ROCHE

Actually, it's in the billions

For more than 15 years, you've been satisfied with the wide margin of safety provided by Dalmane.[1-3] And your patients have been satisfied because they fall asleep quickly and stay asleep till morning.[2,3] As always, caution patients about driving or drinking alcohol.

DALMANE®

flurazepam HCl/Roche Ⓒ IV

sleep that satisfies

References: 1. Greenblatt DJ, Allen MD, Shader RI: *Clin Pharmacol Ther 21*:355-361, Mar 1977. 2. Kales A, Kales JD: *J Clin Psychopharmacol 3*:140-150, Apr 1983. 3. Tennant FS, *et al:* Symposium on the Treatment of Sleep Disorders, Teleconference, Oct 16, 1984. 4. Kales J, *et al: Clin Pharmacol Ther 12*:691-697, Jul-Aug 1971. 5. Kales A, *et al: Clin Pharmacol Ther 18*:356-363, Sep 1975. 6. Kales A, *et al: Clin Pharmacol Ther 19*:576-583, May 1976. 7. Kales A, *et al: Clin Pharmacol Ther 32*:781-788, Dec 1982. 8. Frost JD Jr, DeLucchi MR: *J Am Geriatr Soc 27*:541-546, Dec 1979. 9. Dement WC, *et al: Behav Med,* pp. 25-31, Oct 1978.

a stronger reason to prescribe Motrin Tablets

New Motrin® 800 TABLETS mg
ibuprofen

Extra-Strength Motrin Tablets— a convenient way to tap the full potential of Motrin:

The newest strength of *Motrin* Tablets

makes treatment easier for arthritis patients who need the doses that provide higher levels of anti-inflammatory activity as well as potent analgesia...just 1 tablet t.i.d. provides 2400 mg/day.

expands the dosage convenience of MOTRIN Tablets—makes it even easier to adjust the dosage of MOTRIN to each patient's needs...the new dosage range of up to 3200 mg/day can be achieved on a q.i.d. regimen. Gastroscopic studies at varying doses show an increased tendency toward gastric irritation at higher doses. However, at comparable doses, gastric irritation is about half that seen with aspirin.

provides economy...patients should pay less for MOTRIN Tablets than comparable dosages of Clinoril, Feldene, or Naprosyn.

provides, above all, the experience-proven efficacy and safety profile of *Motrin.* MOTRIN continues to be America's most often prescribed nonsteroidal anti-inflammatory agent.

Please turn the page for a brief summary of prescribing information.

Upjohn

The Upjohn Company, Kalamazoo, Michigan 49001

Motrin® Tablets
(ibuprofen)

Indications and Usage: Treatment of signs and symptoms of rheumatoid arthritis and osteoarthritis. Relief of mild to moderate pain and primary dysmenorrhea. Safety and efficacy in children are not established.

Contraindications: Anaphylactoid reactions have occurred in individuals hypersensitive to MOTRIN or with the syndrome of nasal polyps, angioedema and bronchospastic reactivity to aspirin or other nonsteroidal anti-inflammatory agents.

Warnings: Peptic ulceration and GI bleeding, sometimes severe, have been reported. Ulceration, perforation and bleeding may end fatally. An association has not been established. Use MOTRIN under close supervision in patients with a history of upper gastrointestinal tract disease, after consulting ADVERSE REACTIONS. In patients with active peptic ulcer and active rheumatoid arthritis, try nonulcerogenic drugs, such as gold. If MOTRIN is used, observe the patient closely for signs of ulcer perforation or GI bleeding.

Chronic studies in rats and monkeys have shown mild renal toxicity with papillary edema and necrosis. Renal papillary necrosis has rarely been shown in humans treated with MOTRIN.

Precautions: Blurred and/or diminished vision, scotomata, and/or changes in color vision have been reported. If these develop, discontinue MOTRIN and the patient should have an ophthalmologic examination, including central visual fields and color vision testing.

Fluid retention and edema have been associated with MOTRIN; use with caution in patients with a history of cardiac decompensation or hypertension. In patients with renal impairment, reduced dosage may be necessary. Prospective studies of MOTRIN safety in patients with chronic renal failure have not been done.

MOTRIN can inhibit **platelet aggregation** and prolong bleeding time. Use with caution in persons with intrinsic coagulation defects and on anticoagulant therapy.

Patients should report signs or symptoms of **gastrointestinal ulceration** or bleeding, blurred vision, skin rash, weight gain, or edema. Patients on prolonged **corticosteroid therapy** should have therapy tapered slowly when MOTRIN is added.

The antipyretic, anti-inflammatory activity of MOTRIN may mask inflammation and fever.

As with other nonsteroidal anti-inflammatory drugs, borderline elevations of liver tests may occur in up to 15% of patients. These abnormalities may progress, may remain essentially unchanged, or may be transient with continued therapy. Meaningful elevations of SGPT or SGOT (AST) occurred in controlled clinical trials in less than 1% of patients. Severe hepatic reactions, including jaundice and cases of fatal hepatitis, have been reported with ibuprofen as with other nonsteroidal anti-inflammatory drugs. If liver disease develops or if systemic manifestations occur (eg, eosinophilia, rash, etc.), MOTRIN should be discontinued.

In cross-study comparisons with 1200 mg to 3200 mg daily for several weeks, a slight dose-response decrease in hemoglobin/hematocrit was noted. The total decrease in hemoglobin usually does not exceed 1 gram.

Drug interactions—*Aspirin:* used concomitantly may decrease MOTRIN blood levels.
Coumarin: bleeding has been reported in patients taking MOTRIN and coumarin.

Pregnancy and nursing mothers: MOTRIN should not be taken during pregnancy or by nursing mothers.

Adverse Reactions: The most frequent type of adverse reaction occurring with MOTRIN is gastrointestinal, of which one or more occurred in 4% to 16% of the patients. Reported side effects were higher at 3200 than at 2400 mg/day or less.

Incidence Greater Than 1% (but less than 3%)—Probable Causal Relationship
Gastrointestinal: Nausea;* epigastric pain;* heartburn;* diarrhea, abdominal distress, nausea and vomiting, indigestion, constipation, abdominal cramps or pain, fullness of GI tract (bloating and flatulence); **Central Nervous System:** Dizziness;* headache, nervousness; **Dermatologic:** Rash* (including maculopapular type), pruritus; **Special Senses:** Tinnitus; **Metabolic/Endocrine:** Decreased appetite; **Cardiovascular:** Edema, fluid retention (generally responds promptly to drug discontinuation; see PRECAUTIONS).

Incidence Less Than 1%—Probable Causal Relationship**
Gastrointestinal: Gastric or duodenal ulcer with bleeding and/or perforation, gastrointestinal hemorrhage, melena, gastritis, hepatitis, jaundice, abnormal liver function tests; **Central Nervous System:** Depression, insomnia, confusion, emotional lability, somnolence, aseptic meningitis with fever and coma; **Dermatologic:** Vesiculobullous eruptions, urticaria, erythema multiforme, Stevens-Johnson syndrome, alopecia; **Special Senses:** Hearing loss, amblyopia (blurred and/or diminished vision, scotomata, and/or changes in color vision) (see PRECAUTIONS); **Hematologic:** Neutropenia, agranulocytosis, aplastic anemia, hemolytic anemia (sometimes Coombs positive), thrombocytopenia with or without purpura, eosinophilia, decreases in hemoglobin and hematocrit (see PRECAUTIONS); **Cardiovascular:** Congestive heart failure in patients with marginal cardiac function, elevated blood pressure, palpitations; **Allergic:** Syndrome of abdominal pain, fever, chills, nausea and vomiting; anaphylaxis; bronchospasm (see CONTRAINDICATIONS); **Renal:** Acute renal failure in patients with pre-existing significantly impaired renal function, decreased creatinine clearance, polyuria, azotemia, cystitis, hematuria; **Miscellaneous:** Dry eyes and mouth, gingival ulcer, rhinitis.

Incidence Less Than 1%—Causal Relationship Unknown**
Gastrointestinal: Pancreatitis; **Central Nervous System:** Paresthesias, hallucinations, dream abnormalities, pseudotumor cerebri; **Dermatologic:** Toxic epidermal necrolysis, photoallergic skin reactions; **Special Senses:** Conjunctivitis, diplopia, optic neuritis, cataracts; **Hematologic:** Bleeding episodes (eg, epistaxis, menorrhagia); **Metabolic/Endocrine:** Gynecomastia, hypoglycemic reaction, acidosis; **Cardiovascular:** Arrhythmias (sinus tachycardia, sinus bradycardia); **Allergic:** Serum sickness, lupus erythematosus syndrome, Henoch-Schönlein vasculitis, angioedema; **Renal:** Renal papillary necrosis.

Overdosage: In cases of acute overdosage, the stomach should be emptied. The drug is acidic and excreted in the urine so alkaline diuresis may be beneficial.

Dosage and Administration: Do not exceed 3200 mg/day.

Rheumatoid arthritis and osteoarthritis: Suggested dosage is 1200 to 3200 mg per day (400, 600 or 800 mg t.i.d. or q.i.d.). The smallest effective dosage should be used. Mild to moderate pain: 400 mg every 4 to 6 hours as necessary.

How Supplied:

MOTRIN Tablets, 400 mg (orange)	MOTRIN Tablets, 600 mg (peach)	MOTRIN Tablets, 800 mg (apricot)
Bottles of 500	Bottles of 500	Bottles of 100
Unit-dose package of 100	Unit-dose package of 100	Bottles of 500
Unit of Use bottles of 100	Unit of Use bottles of 100	

Caution: Federal law prohibits dispensing without prescription. *For additional product information, see your Upjohn representative or consult the package insert.*

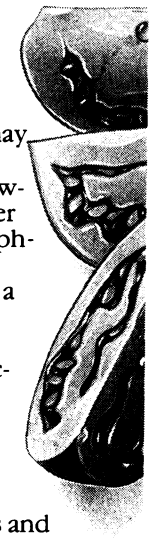
*Reactions occurring in 3% to 9% of patients treated with MOTRIN. (Those reactions occurring in less than 3% of the patients are unmarked.)

**Reactions are classified under *"Probable Causal Relationship (PCR)"* if there has been one positive rechallenge or if three or more cases occur which might be causally related. Reactions are classified under *"Causal Relationship Unknown"* if seven or more events have been reported but the criteria for PCR have not been met.

Upjohn The Upjohn Company
Kalamazoo, Michigan 49001 USA

MED B-8-S
June 1985
J-5503

A defense against cancer can be cooked up in your kitchen.



There is evidence that diet and cancer are related. Some foods may promote cancer, while others may protect you from it.

Foods related to lowering the risk of cancer of the larynx and esophagus all have high amounts of carotene, a form of Vitamin A which is in cantaloupes, peaches, broccoli, spinach, all dark green leafy vegetables, sweet potatoes, carrots, pumpkin, winter squash, and tomatoes, citrus fruits and brussels sprouts.

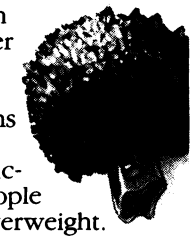
Foods that may help reduce the risk of gastrointestinal and respiratory tract cancer are cabbage, broccoli, brussels sprouts, kohlrabi, cauliflower.

Fruits, vegetables and whole-grain cereals such as oatmeal, bran and wheat may help lower the risk of colorectal cancer.

Foods high in fats, salt- or nitrite-cured foods such as ham, and fish and types of sausages smoked by traditional methods should be eaten in moderation.

Be moderate in consumption of alcohol also.

A good rule of thumb is cut down on fat and don't be fat. Weight reduction may lower cancer risk. Our 12-year study of nearly a million Americans uncovered high cancer risks particularly among people 40% or more overweight.

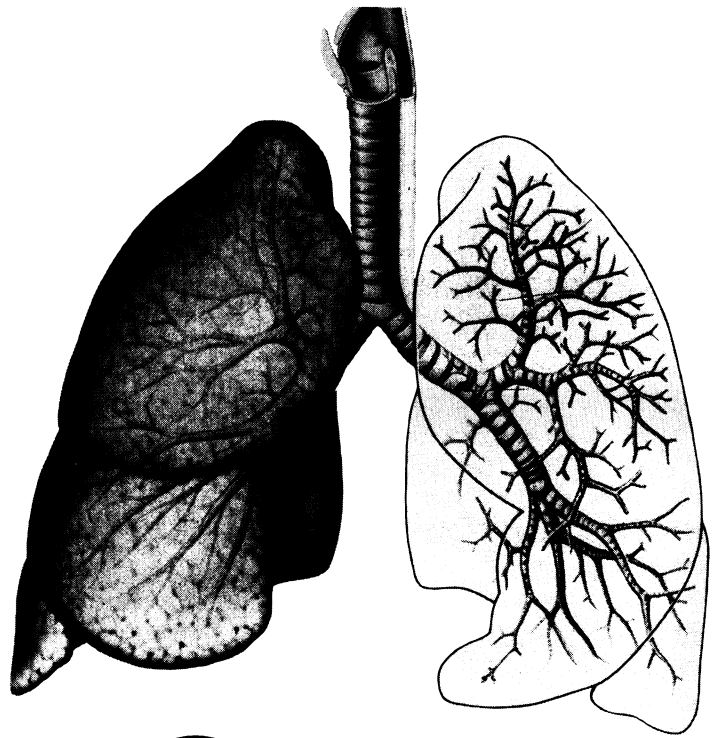


Now, more than ever, we know you can cook up your own defense against cancer. So eat healthy and be healthy.

No one faces cancer alone.

AMERICAN CANCER SOCIETY®

Consider the causative organisms...



Ceclor®
cefaclor
250-mg Pulvules® t.i.d.

offers effectiveness against the major causes of bacterial bronchitis

H. influenzae*, *H. influenzae*, *S. pneumoniae*, *S. pyogenes
(ampicillin-susceptible) (ampicillin-resistant)

Brief Summary. Consult the package literature for prescribing information.

Indications and Usage: Ceclor® (cefaclor, Lilly) is indicated in the treatment of the following infections when caused by susceptible strains of the designated microorganisms:

Lower respiratory infections, including pneumonia caused by *Streptococcus pneumoniae (Diplococcus pneumoniae), Haemophilus influenzae,* and *S. pyogenes* (group A beta-hemolytic streptococci)

Appropriate culture and susceptibility studies should be performed to determine susceptibility of the causative organism to Ceclor.

Contraindication: Ceclor is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

Warnings: IN PENICILLIN-SENSITIVE PATIENTS, CEPHALOSPORIN ANTIBIOTICS SHOULD BE ADMINISTERED CAUTIOUSLY. THERE IS CLINICAL AND LABORATORY EVIDENCE OF PARTIAL CROSS-ALLERGENICITY OF THE PENICILLINS AND THE CEPHALOSPORINS, AND THERE ARE INSTANCES IN WHICH PATIENTS HAVE HAD REACTIONS, INCLUDING ANAPHYLAXIS, TO BOTH DRUG CLASSES.

Antibiotics, including Ceclor, should be administered cautiously to any patient who has demonstrated some form of allergy, particularly to drugs.

Pseudomembranous colitis has been reported with virtually all broad-spectrum antibiotics (including macrolides, semisynthetic penicillins, and cephalosporins); therefore, it is important to consider its diagnosis in patients who develop diarrhea in association with the use of antibiotics. Such colitis may range in severity from mild to life-threatening.

Treatment with broad-spectrum antibiotics alters the normal flora of the colon and may permit overgrowth of clostridia. Studies indicate that a toxin produced by *Clostridium difficile* is one primary cause of antibiotic-associated colitis.

Mild cases of pseudomembranous colitis usually respond to drug discontinuance alone. In moderate to severe cases, management should include sigmoidoscopy, appropriate bacteriologic studies, and fluid, electrolyte, and protein supplementation. When the colitis does not improve after the drug has been discontinued, or when it is severe, oral vancomycin is the drug of choice for antibiotic-associated pseudomembranous colitis produced by *C. difficile.* Other causes of colitis should be ruled out.

Precautions: *General Precautions* — If an allergic reaction to Ceclor® (cefaclor, Lilly) occurs, the drug should be discontinued, and, if necessary, the patient should be treated with appropriate agents, e.g., pressor amines, antihistamines, or corticosteroids.

Prolonged use of Ceclor may result in the overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Positive direct Coombs' tests have been reported during treatment with the cephalosporin antibiotics. In hematologic studies or in transfusion cross-matching procedures when antiglobulin tests are performed on the minor side or in Coombs' testing of newborns whose mothers have received cephalosporin antibiotics before parturition, it should be recognized that a positive Coombs' test may be due to the drug.

Ceclor should be administered with caution in the presence of markedly impaired renal function. Under such conditions, careful clinical observation and laboratory studies should be made because safe dosage may be lower than that usually recommended.

As a result of administration of Ceclor, a false-positive reaction for glucose in the urine may occur. This has been observed with Benedict's and Fehling's solutions and also with Clinitest® tablets but not with Tes-Tape® (Glucose Enzymatic Test Strip, USP, Lilly).

Broad-spectrum antibiotics should be prescribed with caution in individuals with a history of gastrointestinal disease, particularly colitis.

Usage in Pregnancy — Pregnancy Category B — Reproduction studies have been performed in mice and rats at doses up to 12 times the human dose and in ferrets given three times the maximum human dose and have revealed no evidence of impaired fertility or harm to the fetus due to Ceclor® (cefaclor, Lilly). There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers — Small amounts of Ceclor have been detected in mother's milk following administration of single 500-mg doses. Average levels were 0.18, 0.20, 0.21, and 0.16 mcg/ml at two, three, four, and five hours respectively. Trace amounts were detected at one hour. The effect on nursing infants is not known. Caution should be exercised when Ceclor is administered to a nursing woman.

Usage in Children — Safety and effectiveness of this product for use in infants less than one month of age have not been established.

Adverse Reactions: Adverse effects considered related to therapy with Ceclor are uncommon and are listed below:

Gastrointestinal symptoms occur in about 2.5 percent of patients and include diarrhea (1 in 70).

Symptoms of pseudomembranous colitis may appear either during or after antibiotic treatment. Nausea and vomiting have been reported rarely.

Hypersensitivity reactions have been reported in about 1.5 percent of patients and include morbilliform eruptions (1 in 100). Pruritus, urticaria, and positive Coombs' tests each occur in less than 1 in 200 patients. Cases of serum-sickness-like reactions (erythema multiforme or the above skin manifestations accompanied by arthritis/arthralgia and, frequently, fever) have been reported. These reactions are apparently due to hypersensitivity and have usually occurred during or following a second course of therapy with Ceclor. Such reactions have been reported more frequently in children than in adults. Signs and symptoms usually occur a few days after initiation of therapy and subside within a few days after cessation of therapy. No serious sequelae have been reported. Antihistamines and corticosteroids appear to enhance resolution of the syndrome.

Cases of anaphylaxis have been reported, half of which have occurred in patients with a history of penicillin allergy.

Other effects considered related to therapy included eosinophilia (1 in 50 patients) and genital pruritus or vaginitis (less than 1 in 100 patients).

Causal Relationship Uncertain — Transitory abnormalities in clinical laboratory test results have been reported. Although they were of uncertain etiology, they are listed below to serve as alerting information for the physician.

Hepatic — Slight elevations in SGOT, SGPT, or alkaline phosphatase values (1 in 40).

Hematopoietic — Transient fluctuations in leukocyte count, predominantly lymphocytosis occurring in infants and young children (1 in 40).

Renal — Slight elevations in BUN or serum creatinine (less than 1 in 500) or abnormal urinalysis (less than 1 in 200).

[061782R]

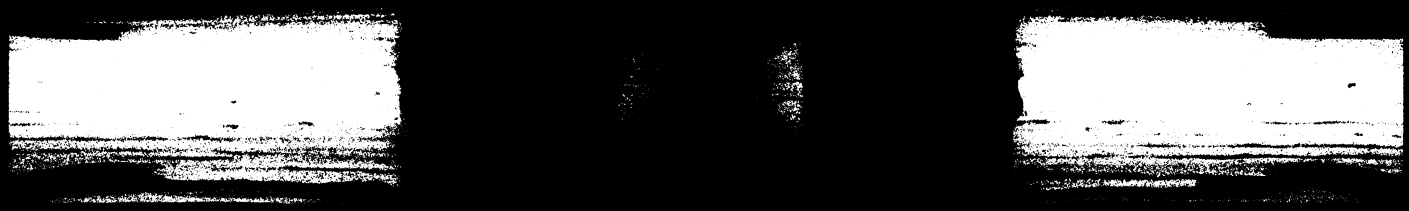
Note: Ceclor® (cefaclor, Lilly) is contraindicated in patients with known allergy to the cephalosporins and should be given cautiously to penicillin-allergic patients.

Penicillin is the usual drug of choice in the treatment and prevention of streptococcal infections, including the prophylaxis of rheumatic fever. See prescribing information.

Additional information available to the profession on request from Eli Lilly and Company, Indianapolis, Indiana 46285

Eli Lilly Industries, Inc.
Carolina, Puerto Rico 00630

400441

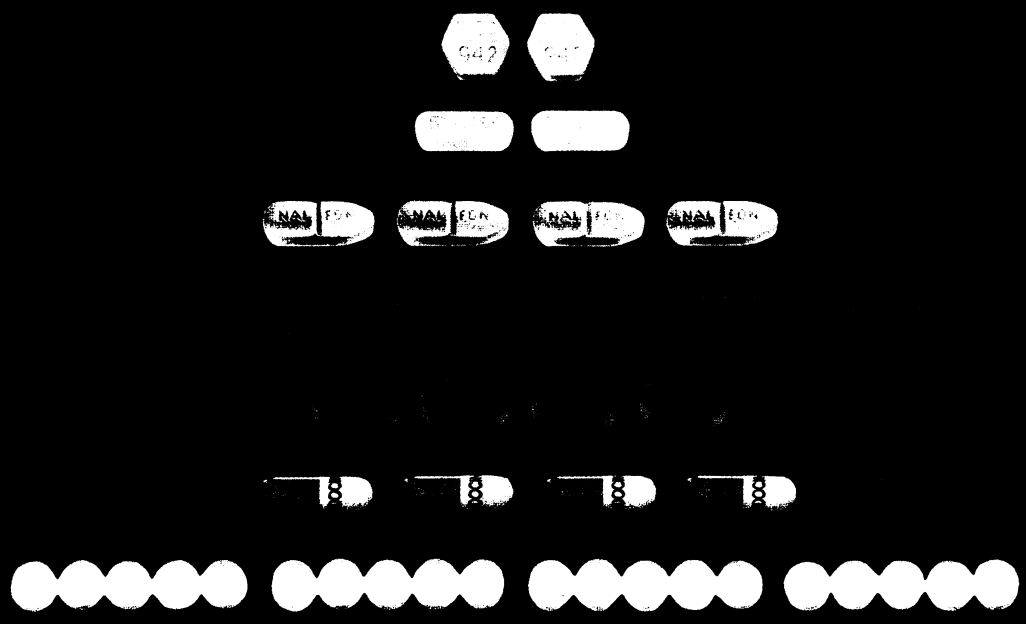


Start one-a-day

For full anti-arthritic action

Start one-a-day

For full anti-arthritic action



Angina comes in many forms...

So does

SORBITRATE®

(ISOSORBIDE DINITRATE)

Unsurpassed flexibility in nitrate therapy.

2.5 mg 5 mg 10 mg
Sublingual Tablets

5 mg 10 mg
Chewable Tablets

5 mg 10 mg 20 mg 30 mg 40 mg
Oral "Swallow" Tablets

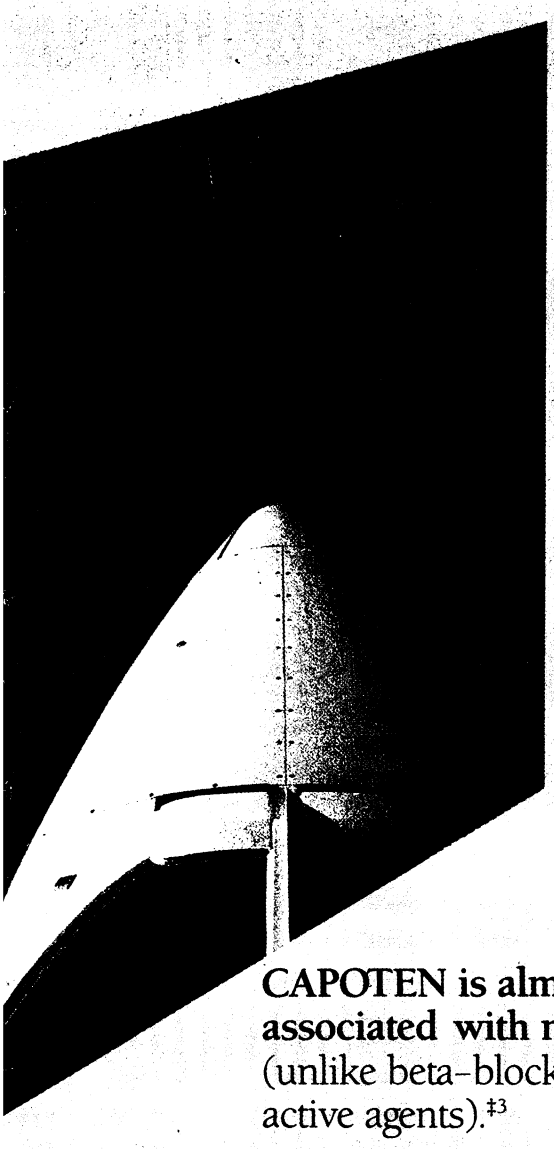
40 mg
Sustained Action "Swallow" Tablets

See previous page for brief summary of prescribing information.

CAPOTEN® (captopril tablets) is almost never associated with fatigue (unlike beta-blockers and CNS active agents: e.g., clonidine, methyldopa).‡[1]

CAPOTEN is almost never associated with loss of libido and impotence (unlike beta-blockers and CNS active agents).‡[1,2]

‡CAPOTEN is indicated for the treatment of hypertensive patients who on multidrug regimens either have failed to respond satisfactorily or have developed unacceptable side effects.
Please see the WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS sections of the brief summary on adjacent pages.



SQUIBB

ACE*INHIBITOR

CAPOTEN® BID
captopril tablets

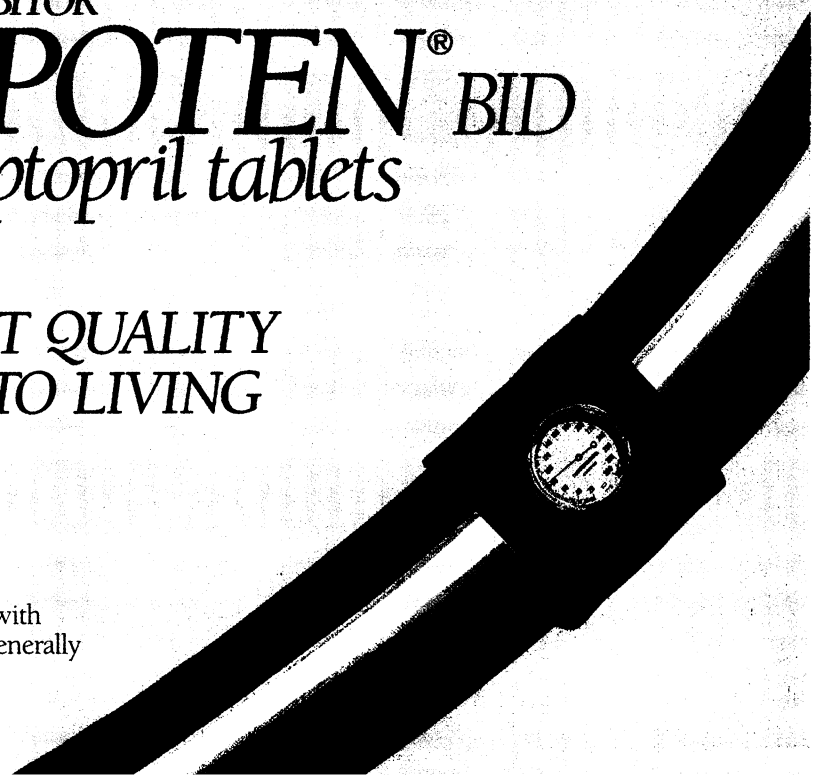
HYPERTENSION CONTROL† PATIENTS CAN FEEL GOOD ABOUT

CAPOTEN is almost never associated with mental impairment (unlike beta-blockers and CNS active agents).‡[3]

ACE*INHIBITOR

CAPOTEN® BID
captopril tablets

HELP PUT QUALITY BACK INTO LIVING



*Angiotensin Converting Enzyme

‡The most frequently occurring adverse reactions associated with CAPOTEN are skin rash and taste alteration; both effects are generally mild, reversible, or self-limited.

ACE*INHIBITOR

CAPOTEN® BID
captopril tablets

Precautionary guidelines

CAPOTEN® (captopril tablets) has been associated with the development of neutropenia/agranulocytosis (0.3% of 4,000 patients) or proteinuria (1.2% of 4,000 patients).† These serious side effects are more likely to occur in patients with predisposing conditions, such as renal impairment or autoimmune disease, or in patients receiving therapy known to suppress the immune response. The following precautionary guidelines are recommended for all patients receiving CAPOTEN:

☐ Obtain urinary protein level estimates prior to initiating therapy, at monthly intervals for the first nine months of treatment, and periodically thereafter.

☐ Obtain WBC counts at the initiation of therapy, at two-week intervals for the first three months of treatment, and periodically thereafter.

☐ Carefully review the WARNINGS and ADVERSE REACTIONS sections in the complete prescribing information, with particular attention to the patient at increased risk.

☐ The most frequently occurring adverse reactions are skin rash and taste alteration; both effects are generally mild, reversible, or self-limited.

References:

1. The 1984 Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure. US Department of Health and Human Services, June 1984.
2. Stevenson JG, Umstead GS: Sexual dysfunction due to antihypertensive agents. Drug Intell Clin Pharm 18:113-121, 1984.
3. Solomon S, Hotchkiss E, Saravay SM, et al: Impairment of memory function by antihypertensive medication. Arch Gen Psychiatry 40:1109-1112, 1983.

*Angiotensin Converting Enzyme

†Please see brief summary for INDICATIONS AND USAGE, WARNINGS, and ADVERSE REACTIONS.

CAPOTEN® TABLETS
Captopril Tablets

INDICATIONS: Hypertension—Because serious adverse effects have been reported (see WARNINGS), CAPOTEN is indicated for treatment of hypertensive patients who on multidrug regimens have either failed to respond satisfactorily or developed unacceptable side effects.

Heart Failure: CAPOTEN (captopril) is indicated in patients with heart failure who have not responded adequately to or cannot be controlled by conventional diuretic and digitalis therapy. CAPOTEN is to be used with diuretics and digitalis.

WARNINGS: Proteinuria—Total urinary proteins >1 g/day were seen in 1.2% of patients on captopril; the nephrotic syndrome occurred in about one-fourth of these cases. About 60% of affected patients had evidence of prior renal disease; the remainder had no known renal dysfunction. In most cases, proteinuria subsided or cleared within 6 months whether or not captopril was continued. The BUN and creatinine were seldom altered in proteinuric patients.

Membranous glomerulopathy was found in nearly all of the proteinuric patients on captopril who were biopsied and may be drug related. Most cases of proteinuria occurred by the eighth month of therapy. Patients should have urinary protein estimates (dip-stick on first morning urine, or quantitative 24-hour urine—the latter provides greater precision when proteinuria is persistent and/or at low levels) before therapy, at approximate monthly intervals for the first nine months of therapy, and periodically thereafter. For patients who develop proteinuria >1 g/day, or increasing proteinuria, the benefits and risks of continuing captopril should be evaluated.

Neutropenia/Agranulocytosis—Neutropenia (<300/mm³) associated with myeloid hypoplasia (probably drug related) occurred in about 0.3% of captopril treated patients. About half of the neutropenic patients developed systemic or oral cavity infections or other features of agranulocytosis. Most of the neutropenic patients had severe hypertension and renal function impairment; about half had systemic lupus erythematosus (SLE), or another autoimmune/collagen disorder; multiple concomitant drug therapy was common, including immunosuppressive therapy in a few cases. Daily doses of captopril in the leukopenic patients were relatively high, particularly in view of their diminished renal function. The neutropenia appeared 3 to 12 weeks after starting captopril; it developed relatively slowly, taking 10 to 30 days to have white blood count fall to its nadir; neutrophils returned to normal in about two weeks (other than two patients who died of sepsis).

Use captopril with caution in patients with impaired renal function, serious autoimmune disease (particularly SLE), or who are exposed to other drugs known to affect the white cells or immune response. In patients at particular risk (as noted above), perform white blood cell and differential counts prior to therapy, at about 2-week intervals for about the first 3 months of therapy, and periodically thereafter.

The risk of neutropenia in patients who are less seriously ill or who receive lower dosages appears to be smaller. In these patients white blood cell counts should be performed every 2 weeks for the first 3 months of therapy, and periodically thereafter. Perform differential counts when leukocytes are <4000/mm³ or the pretherapy white count is halved. All patients treated with captopril should be told to report any signs of infection (e.g., sore throat; fever); if infection is suspected, perform counts without delay. Since discontinuation of captopril and other drugs has generally led to prompt return of the white count to normal, upon confirmation of neutropenia (neutrophil count <1000/mm³) withdraw captopril and closely follow the patient's course.

Hypotension—Excessive hypotension was rarely seen in hypertensive patients but is a possibility in severely salt/volume-depleted persons such as those treated vigorously with diuretics (see PRECAUTIONS [Drug Interactions]).

In heart failure, where blood pressure was either normal or low, transient decreases in mean blood pressure >20% were recorded in about half of the patients. This transient hypotension may occur after any of the first several doses and is usually well tolerated, although rarely it has been associated with arrhythmia or conduction defects. A starting dose of 6.25 or 12.5 mg tid may minimize the hypotensive effect. Patients should be followed closely for the first two weeks of treatment and whenever the dose of captopril and/or diuretic is increased.

BECAUSE OF THE POTENTIAL FALL IN BLOOD PRESSURE IN THESE PATIENTS, THERAPY SHOULD BE STARTED UNDER VERY CLOSE MEDICAL SUPERVISION.

PRECAUTIONS: General: *Impaired Renal Function,* Hypertension—Some hypertensive patients with renal disease, particularly those with severe renal artery stenosis, have developed increases in BUN and serum creatinine. It may be necessary to reduce captopril dosage and/or discontinue diuretic. For some of these patients, normalization of blood pressure and maintenance of adequate renal perfusion may not be possible. Heart Failure—About 20% of patients develop stable elevations of BUN and serum creatinine >20% above normal or baseline upon long-term treatment. Less than 5% of patients, generally with severe preexisting renal disease, required discontinuation due to progressively increasing creatinine. See DOSAGE AND ADMINISTRATION, ADVERSE REACTIONS [Altered Laboratory Findings]. *Valvular Stenosis*—A theoretical concern, for risk of decreased coronary perfusion, has been noted regarding vasodilator treatment in patients with aortic stenosis, due to decreased afterload reduction.

Surgery/Anesthesia—If hypotension occurs during major surgery or anesthesia, and is considered due to the effects of captopril, it is correctable by volume expansion.

Drug Interactions: *Hypotension: Patients on Diuretic Therapy*—Precipitous reduction of blood pressure may occasionally occur within the first 3 hours after administration of the initial captopril dose in patients on diuretics, especially those recently placed on diuretics and those on severe dietary salt restriction or dialysis. This possibility can be minimized by either discontinuing the diuretic or increasing the salt intake about 1 week prior to initiation of captopril therapy. Alternatively, provide medical supervision for at least 3 hours after the initial dose in hypertensive patients.

Agents Having Vasodilator Activity—In heart failure patients vasodilators should be administered with caution.

Agents Causing Renin Release—Captopril's effect will be augmented by antihypertensive agents that cause renin release.

Agents Affecting Sympathetic Activity—The sympathetic nervous system may be especially important in supporting blood pressure in patients receiving captopril alone or with diuretics. Beta-adrenergic blocking drugs add some further antihypertensive effect to captopril, but the overall response is less than additive. Therefore, use agents affecting sympathetic activity (e.g., ganglionic blocking agents or adrenergic neuron blocking agents) with caution.

Agents Increasing Serum Potassium—Give potassium-sparing diuretics or potassium supplements only for documented hypokalemia, and then with caution, since they may lead to a significant increase of serum potassium.

Drug/Laboratory Test Interaction: Captopril may cause a false-positive urine test for acetone.

Carcinogenesis, Mutagenesis and Impairment of Fertility: Two-year studies with doses of 50 to 1350 mg/kg/day in mice and rats failed to show any evidence of carcinogenic potential. Studies in rats have revealed no impairment of fertility.

Usage in Pregnancy: There are no adequate and well-controlled studies in pregnant women. Embryocidal effects were observed in rabbits. Therefore, captopril should be used during pregnancy only if the potential benefit outweighs the potential risk to the fetus.

(continued on next page)

SQUIBB

INNOVATORS IN CARDIOVASCULAR MEDICINE

 525-568 Issued: June 1985

"When it comes to cardiovascular medicine, I like to know exactly what my patients are swallowing."

INDERAL® Tablets

BRAND OF PROPRANOLOL HCl

10 mg 20 mg 40 mg 60 mg 80 mg 90 mg*

BRIEF SUMMARY (FOR FULL PRESCRIBING INFORMATION, SEE PACKAGE CIRCULAR.)

INDERAL® (propranolol hydrochloride) Tablets

CONTRAINDICATIONS

INDERAL is contraindicated in 1) cardiogenic shock, 2) sinus bradycardia and greater than first degree block, 3) bronchial asthma, 4) congestive heart failure (see WARNINGS) unless the failure is secondary to a tachyarrhythmia treatable with INDERAL.

WARNINGS

CARDIAC FAILURE: Sympathetic stimulation may be a vital component supporting circulatory function in patients with congestive heart failure, and its inhibition by beta blockade may precipitate more severe failure. Although beta blockers should be avoided in overt congestive heart failure, if necessary they can be used with close follow-up in patients with a history of failure who are well compensated and are receiving digitalis and diuretics. Beta-adrenergic blocking agents do not abolish the inotropic action of digitalis on heart muscle.

IN PATIENTS WITHOUT A HISTORY OF HEART FAILURE, continued use of beta blockers can, in some cases, lead to cardiac failure. Therefore, at the first sign or symptom of heart failure, the patient should be digitalized and/or treated with diuretics, and the response observed closely, or INDERAL should be discontinued (gradually, if possible).

IN PATIENTS WITH ANGINA PECTORIS, there have been reports of exacerbation of angina and, in some cases, myocardial infarction, following abrupt discontinuance of INDERAL therapy. Therefore, when discontinuance of INDERAL is planned the dosage should be gradually reduced over at least a few weeks and the patient should be cautioned against interruption or cessation of therapy without the physician's advice. If INDERAL therapy is interrupted and exacerbation of angina occurs, it usually is advisable to reinstitute INDERAL therapy and take other measures appropriate for the management of unstable angina pectoris. Since coronary artery disease may be unrecognized, it may be prudent to follow the above advice in patients considered at risk of having occult atherosclerotic heart disease who are given propranolol for other indications.

Nonallergic Bronchospasm (e.g., chronic bronchitis, emphysema)—PATIENTS WITH BRONCHOSPASTIC DISEASES SHOULD IN GENERAL NOT RECEIVE BETA BLOCKERS. INDERAL should be administered with caution since it may block bronchodilation produced by endogenous and exogenous catecholamine stimulation of beta receptors.

MAJOR SURGERY: The necessity or desirability of withdrawal of beta-blocking therapy prior to major surgery is controversial. It should be noted, however, that the impaired ability of the heart to respond to reflex adrenergic stimuli may augment the risks of general anesthesia and surgical procedures.

INDERAL, like other beta blockers, is a competitive inhibitor of beta-receptor agonists and its effects can be reversed by administration of such agents, e.g., dobutamine or isoproterenol. However, such patients may be subject to protracted severe hypotension. Difficulty in starting and maintaining the heartbeat has also been reported with beta blockers.

DIABETES AND HYPOGLYCEMIA: Beta-adrenergic blockade may prevent the appearance of certain premonitory signs and symptoms (pulse rate and pressure changes) of acute hypoglycemia in labile insulin-dependent diabetes. In these patients, it may be more difficult to adjust the dosage of insulin.

THYROTOXICOSIS: Beta blockade may mask certain clinical signs of hyperthyroidism. Therefore, abrupt withdrawal of propranolol may be followed by an exacerbation of symptoms of hyperthyroidism, including thyroid storm. Propranolol does not distort thyroid function tests.

IN PATIENTS WITH WOLFF-PARKINSON-WHITE SYNDROME, several cases have been reported in which, after propranolol, the tachycardia was replaced by a severe bradycardia requiring a demand pacemaker. In one case this resulted after an initial dose of 5 mg propranolol.

PRECAUTIONS

General: Propranolol should be used with caution in patients with impaired hepatic or renal function. INDERAL is not indicated for the treatment of hypertensive emergencies.

Beta-adrenoreceptor blockade can cause reduction of intraocular pressure. Patients should be told that INDERAL (propranolol hydrochloride) may interfere with the glaucoma screening test. Withdrawal may lead to a return of increased intraocular pressure.

Clinical Laboratory Tests: Elevated blood urea levels in patients with severe heart disease, elevated serum transaminase, alkaline phosphatase, lactate dehydrogenase.

DRUG INTERACTIONS: Patients receiving catecholamine-depleting drugs such as reserpine should be closely observed if INDERAL is administered. The added catecholamine-blocking action may produce an excessive reduction of resting sympathetic nervous activity which may result in hypotension, marked bradycardia, vertigo, syncopal attacks, or orthostatic hypotension.

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term studies in animals have been conducted to evaluate toxic effects and carcinogenic potential. In 18-month studies in both rats and mice, employing doses up to 150 mg/kg/day, there was no evidence of significant drug-induced toxicity. There were no drug-related tumorigenic effects at any of the dosage levels. Reproductive studies in animals did not show any impairment of fertility that was attributable to the drug.

Pregnancy: Pregnancy Category C. INDERAL has been shown to be embryotoxic in animal studies at doses about 10 times greater than the maximum recommended human dose.

There are no adequate and well-controlled studies in pregnant women. INDERAL should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: INDERAL is excreted in human milk. Caution should be exercised when INDERAL is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Most adverse effects have been mild and transient and have rarely required the withdrawal of therapy.

Cardiovascular: bradycardia; congestive heart failure; intensification of AV block; hypotension; paresthesia of hands; thrombocytopenic purpura; arterial insufficiency, usually of the Raynaud type.

Central Nervous System: Lightheadedness; mental depression manifested by insomnia, lassitude, weakness, fatigue; reversible mental depression progressing to catatonia; visual disturbances; hallucinations; an acute reversible syndrome characterized by disorientation for time and place, short-term memory loss, emotional lability, slightly clouded sensorium, and decreased performance on neuropsychometrics.

Gastrointestinal: nausea, vomiting, epigastric distress, abdominal cramping, diarrhea, constipation, mesenteric arterial thrombosis, ischemic colitis.

Allergic: pharyngitis and agranulocytosis, erythematous rash, fever combined with aching and sore throat, laryngospasm and respiratory distress.

Respiratory: bronchospasm.

Hematologic: agranulocytosis, nonthrombocytopenic purpura, thrombocytopenic purpura.

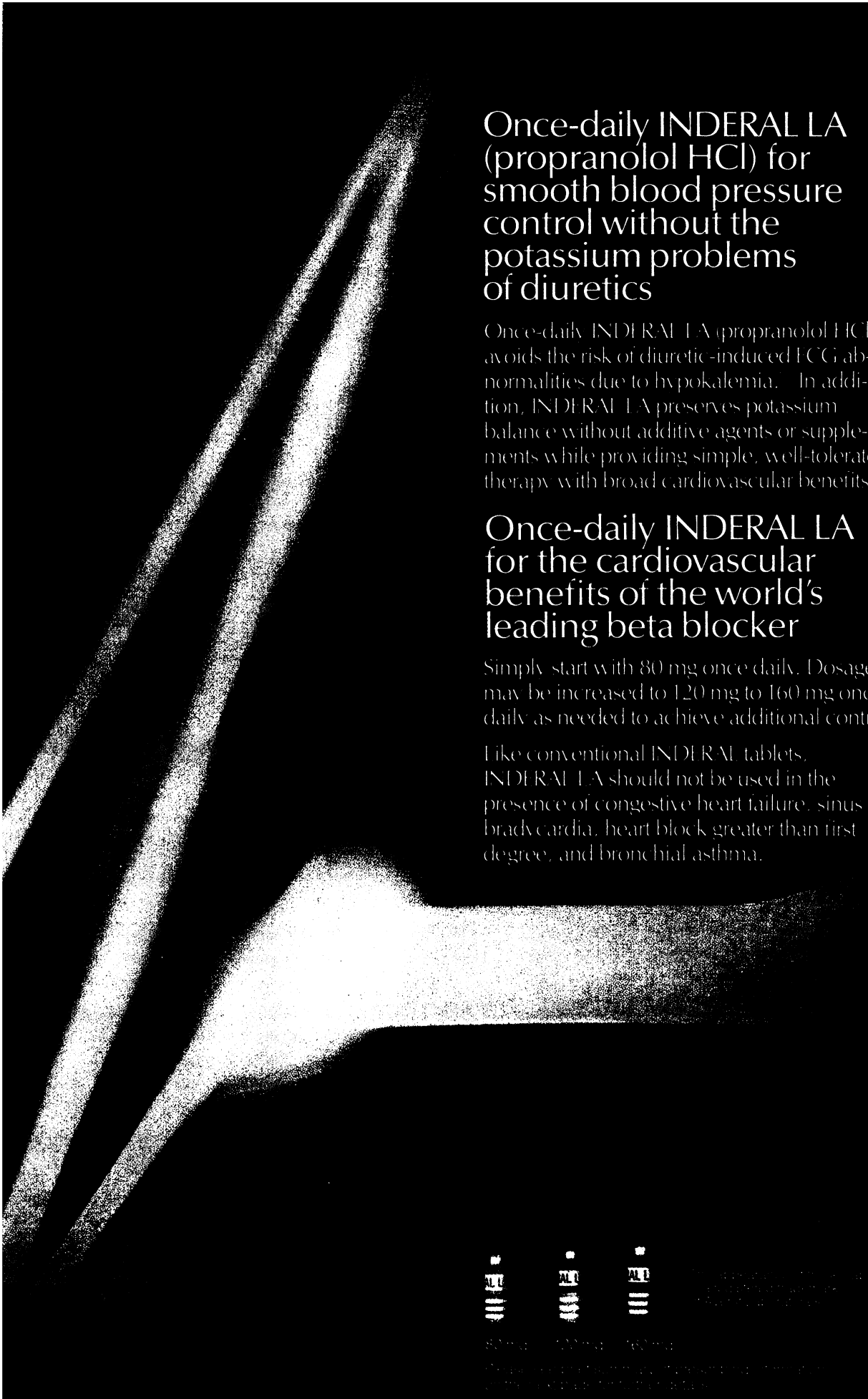
Auto-Immune: In extremely rare instances, systemic lupus erythematosus has been reported.

Miscellaneous: alopecia, LE-like reactions, psoriasiform rashes, dry eyes, male impotence, and Peyronie's disease have been reported rarely. Oculomucocutaneous reactions involving the skin, serous membranes and conjunctivae reported for a beta blocker (practolol) have not been associated with propranolol.

*The appearance of INDERAL tablets is a registered trademark of Ayerst Laboratories.

9429/185

Ayerst® AYERST LABORATORIES
New York, N.Y. 10017



Once-daily INDERAL LA (propranolol HCl) for smooth blood pressure control without the potassium problems of diuretics

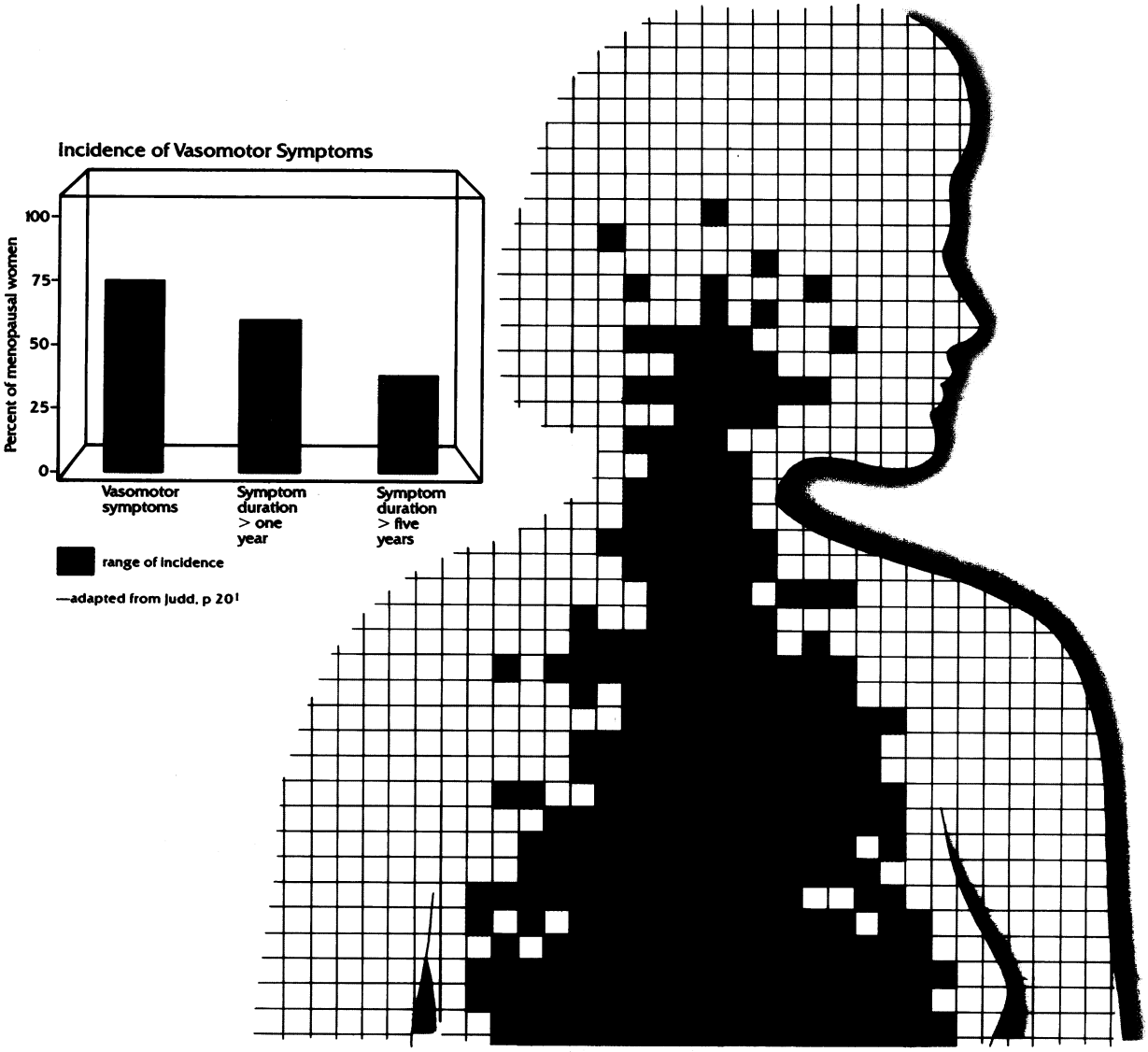
Once-daily INDERAL LA (propranolol HCl) avoids the risk of diuretic-induced ECG abnormalities due to hypokalemia.* In addition, INDERAL LA preserves potassium balance without additive agents or supplements while providing simple, well-tolerated therapy with broad cardiovascular benefits.

Once-daily INDERAL LA for the cardiovascular benefits of the world's leading beta blocker

Simply start with 80 mg once daily. Dosage may be increased to 120 mg to 160 mg once daily as needed to achieve additional control.

Like conventional INDERAL tablets, INDERAL LA should not be used in the presence of congestive heart failure, sinus bradycardia, heart block greater than first degree, and bronchial asthma.

VASOMOTOR SYMPTOMS THAT DEMAND INTERVENTION

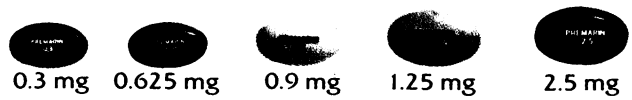


PREMARIN RELIEVES MODERATE TO SEVERE VASOMOTOR SYMPTOMS

Vasomotor symptoms are the most common manifestation of the menopause, affecting up to 75% of menopausal women. Of these, 80% may suffer for more than a year and up to 50% for more than five years.[1] These symptoms can disrupt a woman's life by chronically interrupting sleep, resulting in anxiety and irritability.

In a study of postmenopausal women suffering severe episodes of cutaneous flushing, symptoms improved markedly after administration of estrogen[2]—the treatment of choice for moderate to severe vasomotor symptoms.[3] The estrogen of choice is PREMARIN, the most widely prescribed estrogen for over 40 years. PREMARIN (Conjugated Estrogens Tablets, U.S.P.) relieves moderate to severe vasomotor symptoms of the natural menopause, as well as the acute and often severe symptoms of surgical menopause.

PREMARIN®
(CONJUGATED ESTROGENS TABLETS, U.S.P.)

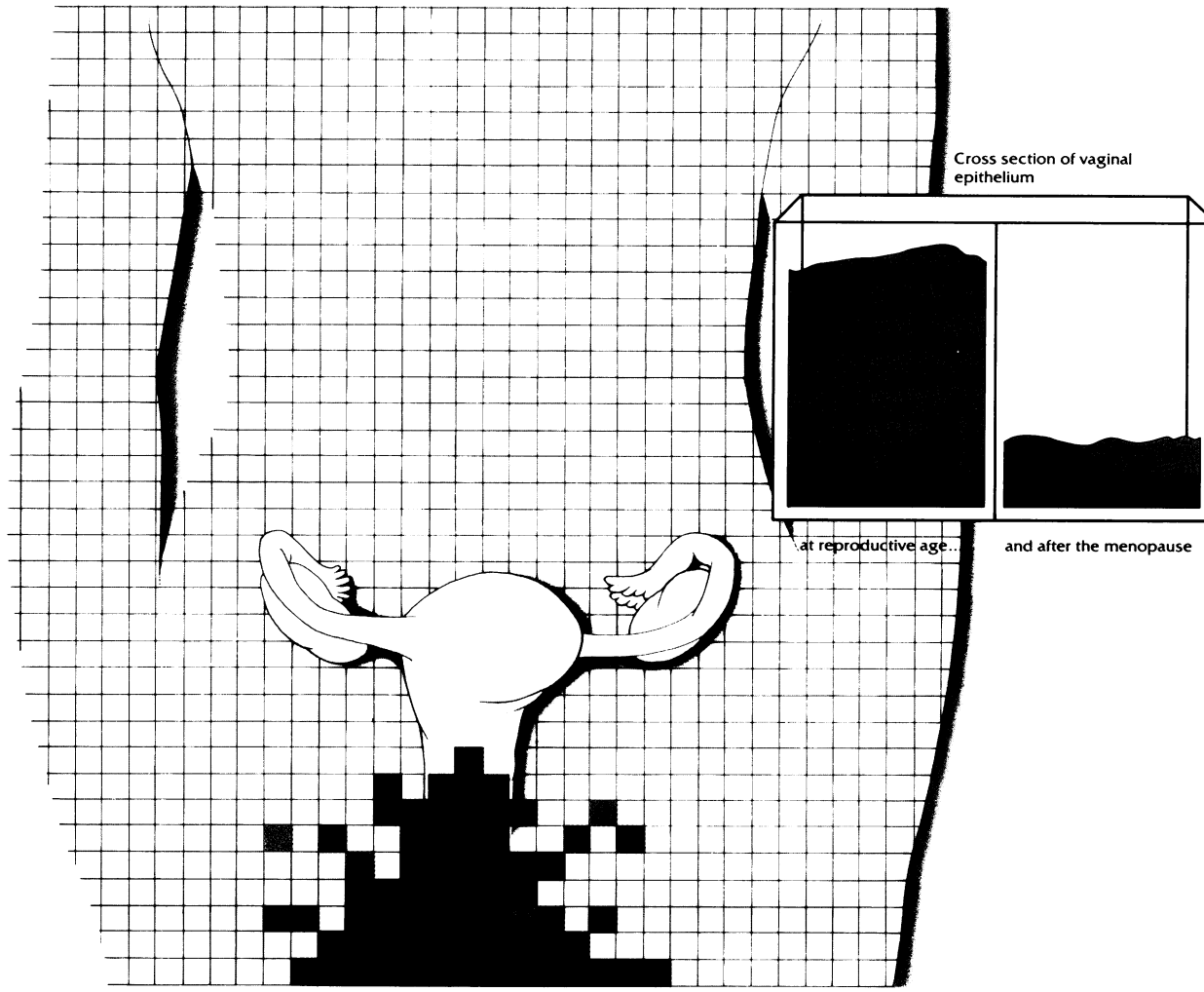


0.3 mg 0.625 mg 0.9 mg 1.25 mg 2.5 mg

The appearance of these tablets is a trademark of Ayerst Laboratories.

Please see last page for brief summary of full prescribing information.

VAGINAL ATROPHY THAT INTERFERES WITH SEXUALITY



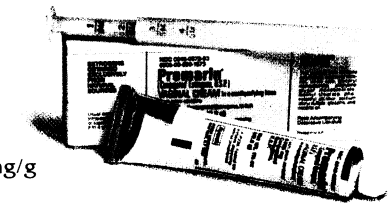
PREMARIN RESTORES THE VAGINAL ENVIRONMENT

In the postmenopausal woman, decreasing levels of estrogen can have devastating effects on a woman's sexual functioning. The pH of vaginal secretions rises, promoting the growth of contaminating organisms. The vaginal epithelium dries and thins, becoming susceptible to irritation, injury, and infection. Sexual relations may be difficult or impossible.

PREMARIN (Conjugated Estrogens, U.S.P.) Vaginal Cream focuses therapy at the site of the problem. Vaginal dryness is relieved, pH reverts to its normal acidity, and the epithelium thickens and becomes more resistant to injury and infection. With the vaginal environment returned to its premenopausal state, sexual function may improve.

PREMARIN®

(CONJUGATED ESTROGENS, U.S.P.) Vaginal Cream

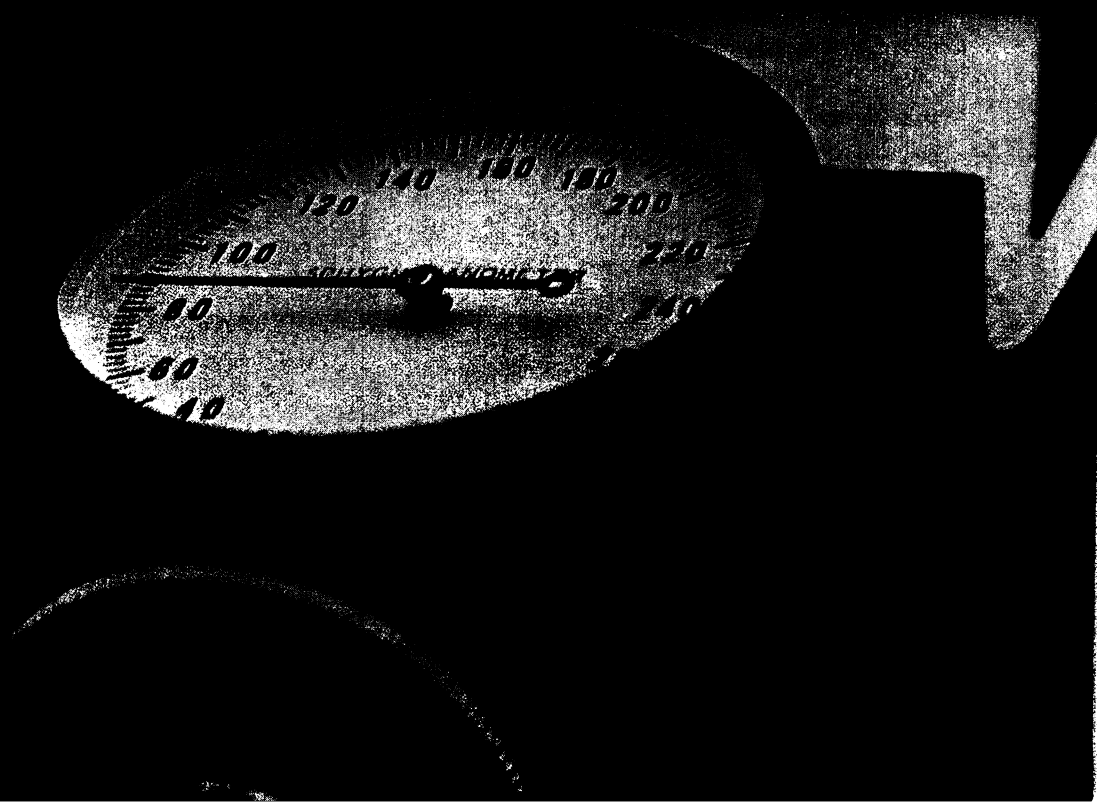


0.625 mg/g

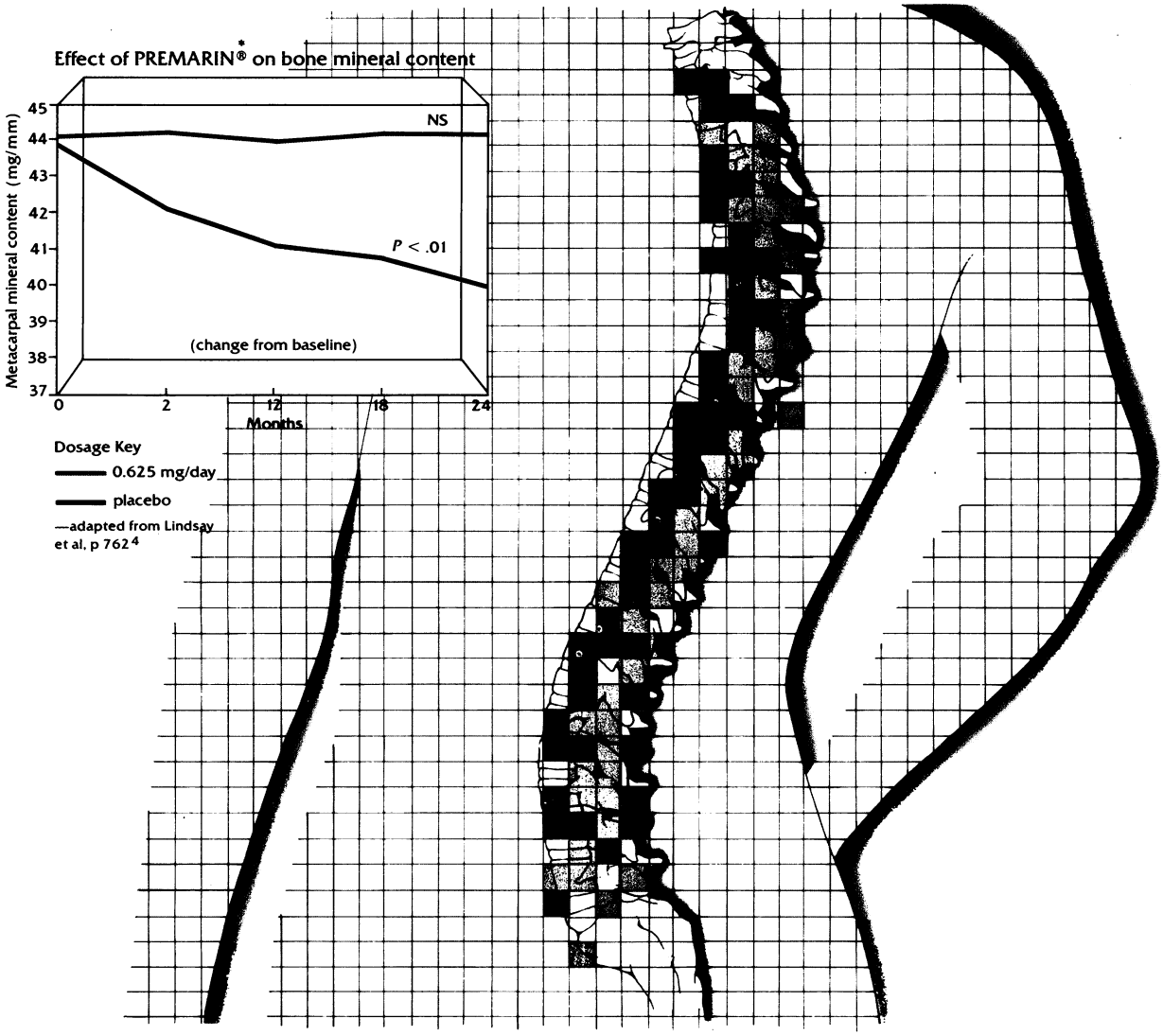
Please see last page for brief summary of full prescribing information.

ANNOUNCING SOME NEW FINDINGS ON CHOLESTEROL.

Right from the start in hypertension...



POSTMENOPAUSAL BONE LOSS THAT INCAPACITATES



PREMARIN MAY HALT THE DISABLING COURSE OF OSTEOPOROSIS*

Osteoporosis has an enormous epidemiological impact: it affects 10 million American women, and 26% of all women over age 60.[5] The disease begins silently and progresses inexorably for 15 to 20 years, until disabling complications occur.[6]

To minimize osteoporotic damage, the condition must be detected early and treated promptly. For many patients, PREMARIN is optimal therapy for osteoporosis, as part of a comprehensive program that includes exercise, good nutrition, and calcium supplements. In a controlled study of postmenopausal and oophorectomized women, PREMARIN (Conjugated Estrogens Tablets, U.S.P.) doses of 0.625 mg/day prevented loss of metacarpal mineral content (see graph above).[4]

PREMARIN®
(CONJUGATED ESTROGENS TABLETS, U.S.P.)

0.3 mg 0.625 mg 0.9 mg 1.25 mg 2.5 mg

The appearance of these tablets is a trademark of Ayerst Laboratories.

*Conjugated Estrogens Tablets have been evaluated as probably effective for estrogen-deficiency-induced osteoporosis.

Please see last page for brief summary of full prescribing information.

BRIEF SUMMARY *(FOR FULL PRESCRIBING INFORMATION AND PATIENT INFORMATION, SEE PACKAGE CIRCULAR)*

PREMARIN® Brand of Conjugated Estrogens Tablets, U.S.P.

PREMARIN® Brand of Conjugated Estrogens, U.S.P. Vaginal Cream in a nonliquefying base

1. ESTROGENS HAVE BEEN REPORTED TO INCREASE THE RISK OF ENDOMETRIAL CARCINOMA.

Three independent case control studies have reported an increased risk of endometrial cancer in postmenopausal women exposed to exogenous estrogens for more than one year. This risk was independent of the other known risk factors for endometrial cancer. These studies are further supported by the finding that incidence rates of endometrial cancer have increased sharply since 1969 in eight different areas of the United States with population-based cancer reporting systems, an increase which may be related to the rapidly expanding use of estrogens during the last decade. The three case control studies reported that the risk of endometrial cancer in estrogen users was about 4.5 to 13.9 times greater than in nonusers. The risk appears to depend on both duration of treatment and on estrogen dose. In view of these findings, when estrogens are used for the treatment of menopausal symptoms, the lowest dose that will control symptoms should be utilized and medication should be discontinued as soon as possible. When prolonged treatment is medically indicated, the patient should be reassessed on at least a semiannual basis to determine the need for continued therapy. Although the evidence must be considered preliminary, one study suggests that cyclic administration of low doses of estrogen may carry less risk than continuous administration; it therefore appears prudent to utilize such a regimen. Close clinical surveillance of all women taking estrogens is important. In all cases of undiagnosed persistent or recurring abnormal vaginal bleeding, adequate diagnostic measures should be undertaken to rule out malignancy. There is no evidence at present that "natural" estrogens are more or less hazardous than "synthetic" estrogens at equiestrogenic doses.

2. ESTROGENS SHOULD NOT BE USED DURING PREGNANCY.

The use of female sex hormones, both estrogens and progestogens, during early pregnancy may seriously damage the offspring. It has been shown that females exposed in utero to diethylstilbestrol, a non-steroidal estrogen, have an increased risk of developing in later life a form of vaginal or cervical cancer that is ordinarily extremely rare. This risk has been estimated as not greater than 4 per 1000 exposures. Furthermore, a high percentage of such exposed women (from 30 to 90 percent) have been found to have vaginal adenosis, epithelial changes of the vagina and cervix. Although these changes are histologically benign, it is not known whether they are precursors of malignancy. Although similar data are not available with the use of other estrogens, it cannot be presumed they would not induce similar changes. Several reports suggest an association between intrauterine exposure to female sex hormones and congenital anomalies, including congenital heart defects and limb reduction defects. One case control study estimated a 4.7-fold increased risk of limb reduction defects in infants exposed in utero to sex hormones (oral contraceptives, hormone withdrawal tests for pregnancy, or attempted treatment for threatened abortion). Some of these exposures were very short and involved only a few days of treatment. The data suggest that the risk of limb reduction defects in exposed fetuses is somewhat less than 1 per 1000. In the past, female sex hormones have been used during pregnancy in an attempt to treat threatened or habitual abortion. There is considerable evidence that estrogens are ineffective for these indications, and there is no evidence from well controlled studies that progestogens are effective for these uses. If PREMARIN is used during pregnancy, or if the patient becomes pregnant while taking this drug, she should be apprised of the potential risks to the fetus, and the advisability of pregnancy continuation.

DESCRIPTION: PREMARIN (Conjugated Estrogens, U.S.P.) contains a mixture of estrogens, obtained exclusively from natural sources, blended to represent the average composition of material derived from pregnant mares' urine. It contains estrone, equilin, and 17α-dihydroequilin, together with smaller amounts of 17α-estradiol, equilenin, and 17α-dihydroequilenin as salts of their sulfate esters.

INDICATIONS: Based on a review of PREMARIN Tablets by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications for use as follows:

Effective: 1. Moderate to severe vasomotor symptoms associated with the menopause. (There is no evidence that estrogens are effective for nervous symptoms or depression without associated vasomotor symptoms, and they should not be used to treat such conditions.)

2. Atrophic vaginitis
3. Kraurosis vulvae
4. Female hypogonadism
5. Female castration
6. Primary ovarian failure
7. Breast cancer (for palliation only) in appropriately selected women and men with metastatic disease.
8. Prostatic carcinoma—palliative therapy of advanced disease.
9. Postpartum breast engorgement—Although estrogens have been widely used for the prevention of postpartum breast engorgement, controlled studies have demonstrated that the incidence of significant painful engorgement in patients not receiving such hormonal therapy is low and usually responsive to appropriate analgesic or other supportive therapy. Consequently, the benefit to be derived from estrogen therapy for this indication must be carefully weighed against the potential increased risk of puerperal thromboembolism associated with the use of large doses of estrogens.

PREMARIN HAS NOT BEEN SHOWN TO BE EFFECTIVE FOR ANY PURPOSE DURING PREGNANCY AND ITS USE MAY CAUSE SEVERE HARM TO THE FETUS (SEE BOXED WARNING).

"Probably" effective: For estrogen deficiency-induced osteoporosis, and only when used in conjunction with other important therapeutic measures such as diet, calcium, physiotherapy, and good general health-promoting measures. Final classification of this indication requires further investigation.

INDICATIONS: PREMARIN (Conjugated Estrogens, U.S.P.) Vaginal Cream is indicated in the treatment of atrophic vaginitis and kraurosis vulvae. PREMARIN Vaginal Cream HAS NOT BEEN SHOWN TO BE EFFECTIVE FOR ANY PURPOSE DURING PREGNANCY AND ITS USE MAY CAUSE SEVERE HARM TO THE FETUS (SEE BOXED WARNING).

CONTRAINDICATIONS: Estrogens should not be used in women (or men) with any of the following conditions: 1. Known or suspected cancer of the breast except in appropriately selected patients being treated for metastatic disease. 2. Known or suspected estrogen-dependent neoplasia. 3. Known or suspected pregnancy (See Boxed Warning). 4. Undiagnosed abnormal genital bleeding. 5. Active thrombophlebitis or thromboembolic disorders. 6. A past history of thrombophlebitis, thrombosis, or thromboembolic disorders associated with previous estrogen use (except when used in treatment of breast or prostatic malignancy).

WARNINGS: Long term continuous administration of natural and synthetic estrogens in certain animal species increases the frequency of carcinomas of the breast, cervix, vagina, and liver. There are now reports that estrogens increase the risk of carcinoma of the endometrium in humans. (See Boxed Warning.) At the present time there is no satisfactory evidence that estrogens given to postmenopausal women increase the risk of cancer of the breast, although a recent study has raised this possibility. There is a need for caution in prescribing estrogens for women with a strong family history of breast cancer or who have breast nodules, fibrocystic disease, or abnormal mammograms. A recent study has reported a 2- to 3-fold increase in the risk of surgically confirmed gallbladder disease in women receiving postmenopausal estrogens.

Adverse effects of oral contraceptives may be expected at the larger doses of estrogen used to treat prostatic or breast cancer or postpartum breast engorgement; it has been shown that there is an increased risk of thrombosis in men receiving estrogens for prostatic cancer and women for postpartum breast engorgement. Users of oral contraceptives have an increased risk of diseases, such as thrombophlebitis, pulmonary embolism, stroke, and myocardial infarction. Cases of retinal thrombosis, mesenteric thrombosis, and optic neuritis have been reported in oral contraceptive users. An increased risk of postsurgery thromboembolic complications has also been reported in users of oral contraceptives. If feasible, estrogen should be discontinued at least 4 weeks before surgery of the type associated with an increased risk of thromboembolism, or during periods of prolonged immobilization. Estrogens should not be used in persons with active thrombophlebitis, thromboembolic disorders, or in persons with a history of such disorders in association with estrogen use. They should be used with caution in patients with cerebral vascular or coronary artery disease. Large doses (5 mg conjugated estrogens per day), comparable to those used to treat cancer of the prostate and breast have been shown to increase the risk of nonfatal myocardial infarction, pulmonary embolism and thrombophlebitis. When doses of this size are used, any of the thromboembolic and thrombotic adverse effects should be considered a clear risk.

Benign hepatic adenomas should be considered in estrogen users having abdominal pain and tenderness, abdominal mass, or hypovolemic shock. Hepatocellular carcinoma has been reported in women taking estrogen-containing oral contraceptives. Increased blood pressure may occur with use of estrogens in the menopause and blood pressure should be monitored with estrogen use. A worsening of glucose tolerance has been observed in patients on estrogen-containing oral contraceptives. For this reason, diabetic patients should be carefully observed. Estrogens may lead to severe hypercalcemia in patients with breast cancer and bone metastases.

PRECAUTIONS: Physical examination and a complete medical and family history should be taken prior to the initiation of any estrogen therapy with special reference to blood pressure, breasts, abdomen, and pelvic organs, and should include a Papanicolau smear. As a general rule, estrogen should not be prescribed for longer than one year without another physical examination being performed. Conditions influenced by fluid retention such as asthma, epilepsy, migraine, and cardiac or renal dysfunction, require careful observation. Certain patients may develop manifestations of excessive estrogenic stimulation, such as abnormal or excessive uterine bleeding, mastodynia, etc. Prolonged administration of unopposed estrogen therapy has been reported to increase the risk of endometrial hyperplasia in some patients. Oral contraceptives appear to be associated with an increased incidence of mental depression. Patients with a history of depression should be carefully observed. Preexisting uterine leiomyomata may increase in size during estrogen use. The pathologist should be advised of estrogen therapy when relevant specimens are submitted. If jaundice develops in any patient receiving estrogen, the medication should be discontinued while the cause is investigated. Estrogens should be used with care in patients with impaired liver function, renal insufficiency, metabolic bone diseases associated with hypercalcemia, or in young patients in whom bone growth is not complete.

The following changes may be expected with larger doses of estrogen:

a. Increased sulfobromophthalein retention.

b. Increased prothrombin and factors VII, VIII, IX, and X; decreased antithrombin 3; increased norepinephrine-induced platelet aggregability.

c. Increased thyroid binding globulin (TBG) leading to increased circulating total thyroid hormone, as measured by PBI, T4 by column, or T4 by radioimmunoassay. Free T3 resin uptake is decreased, reflecting the elevated TBG; free T4 concentration is unaltered.

d. Impaired glucose tolerance.

e. Decreased pregnanediol excretion.

f. Reduced response to metyrapone test.

g. Reduced serum folate concentration.

h. Increased serum triglyceride and phospholipid concentration.

As a general principle, the administration of any drug to nursing mothers should be done only when clearly necessary since many drugs are excreted in human milk.

ADVERSE REACTIONS: The following have been reported with estrogenic therapy, including oral contraceptives: breakthrough bleeding, spotting, change in menstrual flow; dysmenorrhea; premenstrual-like syndrome; amenorrhea during and after treatment; increase in size of uterine fibromyomata; vaginal candidiasis, change in cervical erosion and in degree of cervical secretion; cystitis-like syndrome; tenderness, enlargement, secretion (of breasts); nausea, vomiting, abdominal cramps, bloating; cholestatic jaundice; chloasma or melasma which may persist when drug is discontinued; erythema multiforme; erythema nodosum; hemorrhagic eruption; loss of scalp hair; hirsutism; steepening of corneal curvature; intolerance to contact lenses; headache, migraine, dizziness, mental depression, chorea; increase or decrease in weight; reduced carbohydrate tolerance; aggravation of porphyria; edema; changes in libido.

ACUTE OVERDOSAGE: May cause nausea, and withdrawal bleeding may occur in females.

DOSAGE AND ADMINISTRATION:

PREMARIN® Brand of Conjugated Estrogens Tablets, U.S.P.

1. *Given cyclically for short-term use only.* For treatment of moderate to severe *vasomotor* symptoms, atrophic vaginitis, or kraurosis vulvae associated with the menopause (0.3 to 1.25 mg or more daily).

The lowest dose that will control symptoms should be chosen and medication should be discontinued as promptly as possible.

Administration should be cyclic (*e.g.*, three weeks on and one week off).

Attempts to discontinue or taper medication should be made at three to six month intervals.

2. *Given cyclically:* Female hypogonadism. Female castration. Primary ovarian failure. Osteoporosis.

Female hypogonadism—2.5 to 7.5 mg daily, in divided doses for 20 days, followed by a rest period of 10 days' duration. If bleeding does not occur by the end of this period, the same dosage schedule is repeated. The number of courses of estrogen therapy necessary to produce bleeding may vary depending on the responsiveness of the endometrium.

If bleeding occurs before the end of the 10 day period, begin a 20 day estrogen-progestin cyclic regimen with PREMARIN (Conjugated Estrogens Tablets, U.S.P.), 2.5 to 7.5 mg daily in divided doses, for 20 days. During the last five days of estrogen therapy, give an oral progestin. If bleeding occurs before this regimen is concluded, therapy is discontinued and may be resumed on the fifth day of bleeding.

Female castration and primary ovarian failure—1.25 mg daily, cyclically. Adjust upward or downward according to response of the patient. For maintenance, adjust dosage to lowest level that will provide effective control.

Osteoporosis (to retard progression)—1.25 mg daily, cyclically.

3. *Given for a few days:* Prevention of postpartum breast engorgement—3.75 mg every four hours for five doses, or 1.25 mg every four hours for five days.

4. *Given chronically:* Inoperable progressing prostatic cancer—1.25 to 2.5 mg three times daily.

Inoperable progressing breast cancer in appropriately selected men and postmenopausal women—10 mg three times daily for a period of at least three months.

Patients with an intact uterus should be monitored for signs of endometrial cancer and appropriate measures taken to rule out malignancy in the event of persistent or recurring abnormal vaginal bleeding.

PREMARIN® Brand of Conjugated Estrogens, U.S.P. Vaginal Cream

Given cyclically for short-term use only. For treatment of atrophic vaginitis or kraurosis vulvae.

The lowest dose that will control symptoms should be chosen and medication should be discontinued as promptly as possible.

Administration should be cyclic (*e.g.*, three weeks on and one week off).

Attempts to discontinue or taper medication should be made at three to six month intervals.

Usual dosage range: 2 to 4 g daily, intravaginally or topically, depending on the severity of the condition.

Treated patients with an intact uterus should be monitored closely for signs of endometrial cancer and appropriate diagnostic measures should be taken to rule out malignancy in the event of persistent or recurring abnormal vaginal bleeding.

HOW SUPPLIED: PREMARIN (Conjugated Estrogens Tablets, U.S.P.). No. 865—Each *purple* tablet contains 2.5 mg in bottles of 100 and 1,000. No. 866—Each *yellow* tablet contains 1.25 mg in bottles of 100 and 1,000. Also in Cycle Pack of 21 and in unit dose package of 100. No. 864—Each *white* tablet contains 0.9 mg in bottles of 100. Also in Cycle Pack of 21. No. 867—Each *maroon* tablet contains 0.625 mg in bottles of 100 and 1,000. Also in Cycle Pack of 21 and unit dose package of 100. No. 868—Each *green* tablet contains 0.3 mg in bottles of 100 and 1,000. The appearance of these tablets is a trademark of Ayerst Laboratories.

PREMARIN (Conjugated Estrogens, U.S.P.) Vaginal Cream—No. 872—Each gram contains 0.625 mg Conjugated Estrogens, U.S.P. (Also contains cetyl esters wax, cetyl alcohol, white wax, glyceryl monostearate, propylene glycol monostearate, methyl stearate, phenylethyl alcohol, sodium lauryl sulfate, glycerin, and mineral oil.)

Combination package: Each contains Net Wt. 1½ oz. (42.5 g) tube with one calibrated plastic applicator.

Also Available—Refill package: Each contains Net Wt. 1½ oz. (42.5 g) tube. **4340R2/785**

REFERENCES: 1. Judd HL: After the menopause. *Transition* 1983;1:19-30. 2. Erlik Y, Tataryn IV, Meldrum DR, et al: Association of waking episodes with menopausal hot flushes. *JAMA* 1981;245:1741-1744. 3. Meldrum DR: The pathophysiology of postmenopausal symptoms. *Sem Reprod Endocrinol* 1983;1(February):11-17. 4. Lindsay R, Hart DM, Clark DM: The minimum effective dose of estrogen for prevention of postmenopausal bone loss. *Obstet Gynecol* 1984;63:759-763. 5. Katz WA: *Rheumatic Diseases: Diagnosis and Management*. Philadelphia, JB Lippincott Co, 1977, p 672. 6. Reese WD: A better way to screen for osteoporosis. *Contemp Ob/Gyn* 1983;22(November):116-131.

Ayerst® AYERST LABORATORIES
New York, N.Y. 10017

California Medical Association Regional Postgraduate Institutes

NEW PROGRAMS

West Coast Counties
Monterey Sheraton
October 24-26, 1985

San Joaquin Valley Counties
Curry Village, Yosemite
April 17-19, 1986

TOPICS

- Practical Dermatology
- Update on AIDS
- Update on Hepatitis
- Current Antibiotic Therapy
- Quackery and Cancer in California
- Diabetes Management
- Cancer Chemotherapy
- Issues in Immunization
- Update for Primary Care Physicians

The content of these programs has been determined by the educational needs of primary care physicians as perceived and translated by the members of the Planning Committee.

***

These programs are accredited for Category One credit for Physicians and Registered Nurses

***

Hotel space is limited — early reservations are suggested.

***

Complete program and hotel information will be sent by return mail.
Use the tear off sheet below or call CMA 415/863-5522, extension 416.

WJ08/85

I plan to attend the following Postgraduate Institute(s):

☐ West Coast Counties
October 24-26, 1985
Monterey Sheraton

☐ San Joaquin Valley Counties
April 17-19, 1986
Curry Village, Yosemite

FEE: $125 for each institute
($200 for Non-CMA members)

Please make check payable to
California Medical Association

Name _____ Specialty _____
Address _____
City _____ Zip _____
Number of years out of medical school _____

Mail to: California Medical Association, 44 Gough Street, San Francisco, CA 94103
Attention: Janice Rigney

A program and hotel reservation form will be sent to you.

BALANCED CALCIUM CHANNEL BLOCKER

Low incidence of side effects
CARDIZEM® (diltiazem HCl) produces an incidence of adverse reactions not greater than that reported with placebo therapy, thus contributing to the patient's sense of well-being.

*Cardizem is indicated in the treatment of angina pectoris due to coronary artery spasm and in the management of chronic stable angina (classic effort-associated angina) in patients who cannot tolerate therapy with beta-blockers and/or nitrates or who remain symptomatic despite adequate doses of these agents.

References:
1. Strauss WE, McIntyre KM, Parisi AF, et al: Safety and efficacy of diltiazem hydrochloride for the treatment of stable angina pectoris: Report of a cooperative clinical trial. Am J Cardiol 49:660-666, 1982.
2. Pool PE, Seagren SC, Bonanno JA, et al: The treatment of exercise-inducible chronic stable angina with diltiazem: Effect on treadmill exercise. Chest 78 (July suppl):234-238, 1980.

Reduces angina attack frequency*
42% to 46% decrease reported in multicenter study.[1]

Increases exercise tolerance*
In Bruce exercise test,[2] control patients averaged 8.0 minutes to onset of pain; Cardizem patients averaged 9.8 minutes ($P<.005$).

CARDIZEM®
(diltiazem HCl)

THE BALANCED CALCIUM CHANNEL BLOCKER

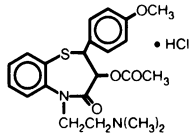
Please see full prescribing information on following page.

PROFESSIONAL USE INFORMATION

cardizem®
(diltiazem HCl)
30 mg and 60 mg tablets

DESCRIPTION

CARDIZEM® (diltiazem hydrochloride) is a calcium ion influx inhibitor (slow channel blocker or calcium antagonist). Chemically, diltiazem hydrochloride is 1,5-Benzothiazepin-4(5H)one,3-(acetyloxy) -5-[2-(dimethylamino)ethyl]-2,3-dihydro-2-(4-methoxyphenyl)-, monohydrochloride,(+) -cis-. The chemical structure is:



Diltiazem hydrochloride is a white to off-white crystalline powder with a bitter taste. It is soluble in water, methanol, and chloroform. It has a molecular weight of 450.98. Each tablet of CARDIZEM contains either 30 mg or 60 mg diltiazem hydrochloride for oral administration.

CLINICAL PHARMACOLOGY

The therapeutic benefits achieved with CARDIZEM are believed to be related to its ability to inhibit the influx of calcium ions during membrane depolarization of cardiac and vascular smooth muscle.

Mechanisms of Action. Although precise mechanisms of its antianginal actions are still being delineated, CARDIZEM is believed to act in the following ways:

1. Angina Due to Coronary Artery Spasm: CARDIZEM has been shown to be a potent dilator of coronary arteries both epicardial and subendocardial. Spontaneous and ergonovine-induced coronary artery spasm are inhibited by CARDIZEM.
2. Exertional Angina: CARDIZEM has been shown to produce increases in exercise tolerance, probably due to its ability to reduce myocardial oxygen demand. This is accomplished via reductions in heart rate and systemic blood pressure at submaximal and maximal exercise work loads.

In animal models, diltiazem interferes with the slow inward (depolarizing) current in excitable tissue. It causes excitation-contraction uncoupling in various myocardial tissues without changes in the configuration of the action potential. Diltiazem produces relaxation of coronary vascular smooth muscle and dilation of both large and small coronary arteries at drug levels which cause little or no negative inotropic effect. The resultant increases in coronary blood flow (epicardial and subendocardial) occur in ischemic and nonischemic models and are accompanied by dose-dependent decreases in systemic blood pressure and decreases in peripheral resistance.

Hemodynamic and Electrophysiologic Effects. Like other calcium antagonists, diltiazem decreases sinoatrial and atrioventricular conduction in isolated tissues and has a negative inotropic effect in isolated preparations. In the intact animal, prolongation of the AH interval can be seen at higher doses.

In man, diltiazem prevents spontaneous and ergonovine-provoked coronary artery spasm. It causes a decrease in peripheral vascular resistance and a modest fall in blood pressure and, in exercise tolerance studies in patients with ischemic heart disease, reduces the heart rate-blood pressure product for any given work load. Studies to date, primarily in patients with good ventricular function, have not revealed evidence of a negative inotropic effect; cardiac output, ejection fraction, and left ventricular end diastolic pressure have not been affected. There are as yet few data on the interaction of diltiazem and beta-blockers. Resting heart rate is usually unchanged or slightly reduced by diltiazem.

Intravenous diltiazem in doses of 20 mg prolongs AH conduction time and AV node functional and effective refractory periods approximately 20%. In a study involving single oral doses of 300 mg of CARDIZEM in six normal volunteers, the average maximum PR prolongation was 14% with no instances of greater than first-degree AV block. Diltiazem-associated prolongation of the AH interval is not more pronounced in patients with first-degree heart block. In patients with sick sinus syndrome, diltiazem significantly prolongs sinus cycle length (up to 50% in some cases).

Chronic oral administration of CARDIZEM in doses of up to 240 mg/day has resulted in small increases in PR interval, but has not usually produced abnormal prolongation. There were, however, three instances of second-degree AV block and one instance of third-degree AV block in a group of 959 chronically treated patients.

Pharmacokinetics and Metabolism. Diltiazem is absorbed from the tablet formulation to about 80% of a reference capsule and is subject to an extensive first-pass effect, giving an absolute bioavailability (compared to intravenous dosing) of about 40%. CARDIZEM undergoes extensive hepatic metabolism in which 2% to 4% of the unchanged drug appears in the urine. In vitro binding studies show CARDIZEM is 70% to 80% bound to plasma proteins. Competitive ligand binding studies have also shown CARDIZEM binding is not altered by therapeutic concentrations of digoxin, hydrochlorothiazide, phenylbutazone, propranolol, salicylic acid, or warfarin. Single oral doses of 30 to 120 mg of CARDIZEM result in detectable plasma levels within 30 to 60 minutes and peak plasma levels two to three hours after drug administration. The plasma elimination half-life following single or multiple drug administration is approximately 3.5 hours. Desacetyl diltiazem is also present in the plasma at levels of 10% to 20% of the parent drug and is 25% to 50% as potent a coronary vasodilator as diltiazem. Therapeutic blood levels of CARDIZEM appear to be in the range of 50 to 200 ng/ml. There is a departure from dose-linearity when single doses above 60 mg are given; a 120-mg dose gave blood levels three times that of the 60-mg dose. There is no information about the effect of renal or hepatic impairment on excretion or metabolism of diltiazem.

INDICATIONS AND USAGE

1. **Angina Pectoris Due to Coronary Artery Spasm.** CARDIZEM is indicated in the treatment of angina pectoris due to coronary artery spasm. CARDIZEM has been shown effective in the treatment of spontaneous coronary artery spasm presenting as Prinzmetal's variant angina (resting angina with ST-segment elevation occurring during attacks).
2. **Chronic Stable Angina (Classic Effort-Associated Angina).** CARDIZEM is indicated in the management of chronic stable angina. CARDIZEM has been effective in controlled trials in reducing angina frequency and increasing exercise tolerance.

There are no controlled studies of the effectiveness of the concomitant use of diltiazem and beta-blockers or of the safety of this combination in patients with impaired ventricular function or conduction abnormalities.

CONTRAINDICATIONS

CARDIZEM is contraindicated in (1) patients with sick sinus syndrome except in the presence of a functioning ventricular pacemaker, (2) patients with second- or third-degree AV block except in the presence of a functioning ventricular pacemaker, and (3) patients with hypotension (less than 90 mm Hg systolic).

WARNINGS

1. **Cardiac Conduction.** CARDIZEM prolongs AV node refractory periods without significantly prolonging sinus node recovery time, except in patients with sick sinus syndrome. This effect may rarely result in abnormally slow heart rates (particularly in patients with sick sinus syndrome) or second- or third-degree AV block (six of 1243 patients for 0.48%). Concomitant use of diltiazem with beta-blockers or digitalis may result in additive effects on cardiac conduction. A patient with Prinzmetal's angina developed periods of asystole (2 to 5 seconds) after a single dose of 60 mg of diltiazem.
2. **Congestive Heart Failure.** Although diltiazem has a negative inotropic effect in isolated animal tissue preparations, hemodynamic studies in humans with normal ventricular function have not shown a reduction in cardiac index nor consistent negative effects on contractility (dp/dt). Experience with the use of CARDIZEM alone or in combination with beta-blockers in patients with impaired ventricular function is very limited. Caution should be exercised when using the drug in such patients.
3. **Hypotension.** Decreases in blood pressure associated with CARDIZEM therapy may occasionally result in symptomatic hypotension.
4. **Acute Hepatic Injury.** In rare instances, patients receiving CARDIZEM have exhibited reversible acute hepatic injury as evidenced by moderate to extreme elevations of liver enzymes. (See PRECAUTIONS and ADVERSE REACTIONS.)

PRECAUTIONS

General. CARDIZEM (diltiazem hydrochloride) is extensively metabolized by the liver and excreted by the kidneys and in bile. As with any new drug given over prolonged periods, laboratory parameters should be monitored at regular intervals. The drug should be used with caution in patients with impaired renal or hepatic function. In subacute and chronic dog and rat studies designed to produce toxicity, high doses of diltiazem were associated with hepatic damage. In special subacute hepatic studies, oral doses of 125 mg/kg and higher in rats were associated with histological changes in the liver which were reversible when the drug was discontinued. In dogs, doses of 20 mg/kg were also associated with hepatic changes; however, these changes were reversible with continued dosing.

Drug Interaction. Pharmacologic studies indicate that there may be additive effects in prolonging AV conduction when using beta-blockers or digitalis concomitantly with CARDIZEM. (See WARNINGS).

Controlled and uncontrolled domestic studies suggest that concomitant use of CARDIZEM and beta-blockers or digitalis is usually well tolerated. Available data are not sufficient, however, to predict the effects of concomitant treatment, particularly in patients with left ventricular dysfunction or cardiac conduction abnormalities. In healthy volunteers, diltiazem has been shown to increase serum digoxin levels up to 20%.

Carcinogenesis, Mutagenesis, Impairment of Fertility. A 24-month study in rats and a 21-month study in mice showed no evidence of carcinogenicity. There was also no mutagenic response in in vitro bacterial tests. No intrinsic effect on fertility was observed in rats.

Pregnancy. Category C. Reproduction studies have been conducted in mice, rats, and rabbits. Administration of doses ranging from five to ten times greater (on a mg/kg basis) than the daily recommended therapeutic dose has resulted in embryo and fetal lethality. These doses, in some studies, have been reported to cause skeletal abnormalities. In the perinatal/postnatal studies, there was some reduction in early individual pup weights and survival rates. There was an increased incidence of stillbirths at doses of 20 times the human dose or greater.

There are no well-controlled studies in pregnant women; therefore, use CARDIZEM in pregnant women only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, exercise caution when CARDIZEM is administered to a nursing woman if the drug's benefits are thought to outweigh its potential risks in this situation.

Pediatric Use. Safety and effectiveness in children have not been established.

ADVERSE REACTIONS

Serious adverse reactions have been rare in studies carried out to date, but it should be recognized that patients with impaired ventricular function and cardiac conduction abnormalities have usually been excluded.

In domestic placebo-controlled trials, the incidence of adverse reactions reported during CARDIZEM therapy was not greater than that reported during placebo therapy.

The following represent occurrences observed in clinical studies which can be at least reasonably associated with the pharmacology of calcium influx inhibition. In many cases, the relationship to CARDIZEM has not been established. The most common occurrences, as well as their frequency of presentation, are: edema (2.4%), headache (2.1%), nausea (1.9%), dizziness (1.5%), rash (1.3%), asthenia (1.2%), AV block (1.1%). In addition, the following events were reported infrequently (less than 1%) with the order of presentation corresponding to the relative frequency of occurrence.

Cardiovascular:	Flushing, arrhythmia, hypotension, bradycardia, palpitations, congestive heart failure, syncope.
Nervous System:	Paresthesia, nervousness, somnolence, tremor, insomnia, hallucinations, and amnesia.
Gastrointestinal:	Constipation, dyspepsia, diarrhea, vomiting, mild elevations of alkaline phosphatase, SGOT, SGPT, and LDH.
Dermatologic:	Pruritus, petechiae, urticaria, photosensitivity.
Other:	Polyuria, nocturia.

The following additional experiences have been noted:

A patient with Prinzmetal's angina experiencing episodes of vasospastic angina developed periods of transient asymptomatic asystole approximately five hours after receiving a single 60-mg dose of CARDIZEM.

The following postmarketing events have been reported infrequently in patients receiving CARDIZEM: erythema multiforme; leukopenia; and extreme elevations of alkaline phosphatase, SGOT, SGPT, LDH, and CPK. However, a definitive cause and effect between these events and CARDIZEM therapy is yet to be established.

OVERDOSAGE OR EXAGGERATED RESPONSE

Overdosage experience with oral diltiazem has been limited. Single oral doses of 300 mg of CARDIZEM have been well tolerated by healthy volunteers. In the event of overdosage or exaggerated response, appropriate supportive measures should be employed in addition to gastric lavage. The following measures may be considered:

Bradycardia	Administer atropine (0.60 to 1.0 mg). If there is no response to vagal blockade, administer isoproterenol cautiously.
High-Degree AV Block	Treat as for bradycardia above. Fixed high-degree AV block should be treated with cardiac pacing.
Cardiac Failure	Administer inotropic agents (isoproterenol, dopamine, or dobutamine) and diuretics.
Hypotension	Vasopressors (eg, dopamine or levarterenol bitartrate).

Actual treatment and dosage should depend on the severity of the clinical situation and the judgment and experience of the treating physician.

The oral/LD_{50}'s in mice and rats range from 415 to 740 mg/kg and from 560 to 810 mg/kg, respectively. The intravenous LD_{50}'s in these species were 60 and 38 mg/kg, respectively. The oral LD_{50} in dogs is considered to be in excess of 50 mg/kg, while lethality was seen in monkeys at 360 mg/kg. The toxic dose in man is not known, but blood levels in excess of 800 ng/ml have not been associated with toxicity.

DOSAGE AND ADMINISTRATION

Exertional Angina Pectoris Due to Atherosclerotic Coronary Artery Disease or Angina Pectoris at Rest Due to Coronary Artery Spasm. Dosage must be adjusted to each patient's needs. Starting with 30 mg four times daily, before meals and at bedtime, dosage should be increased gradually (given in divided doses three or four times daily) at one- to two-day intervals until optimum response is obtained. Although individual patients may respond to any dosage level, the average optimum dosage range appears to be 180 to 240 mg/day. There are no available data concerning dosage requirements in patients with impaired renal or hepatic function. If the drug must be used in such patients, titration should be carried out with particular caution.

Concomitant Use With Other Antianginal Agents:

1. **Sublingual NTG** may be taken as required to abort acute anginal attacks during CARDIZEM therapy.
2. **Prophylactic Nitrate Therapy**—CARDIZEM may be safely coadministered with short- and long-acting nitrates, but there have been no controlled studies to evaluate the antianginal effectiveness of this combination.
3. **Beta-blockers.** (See WARNINGS and PRECAUTIONS.)

HOW SUPPLIED

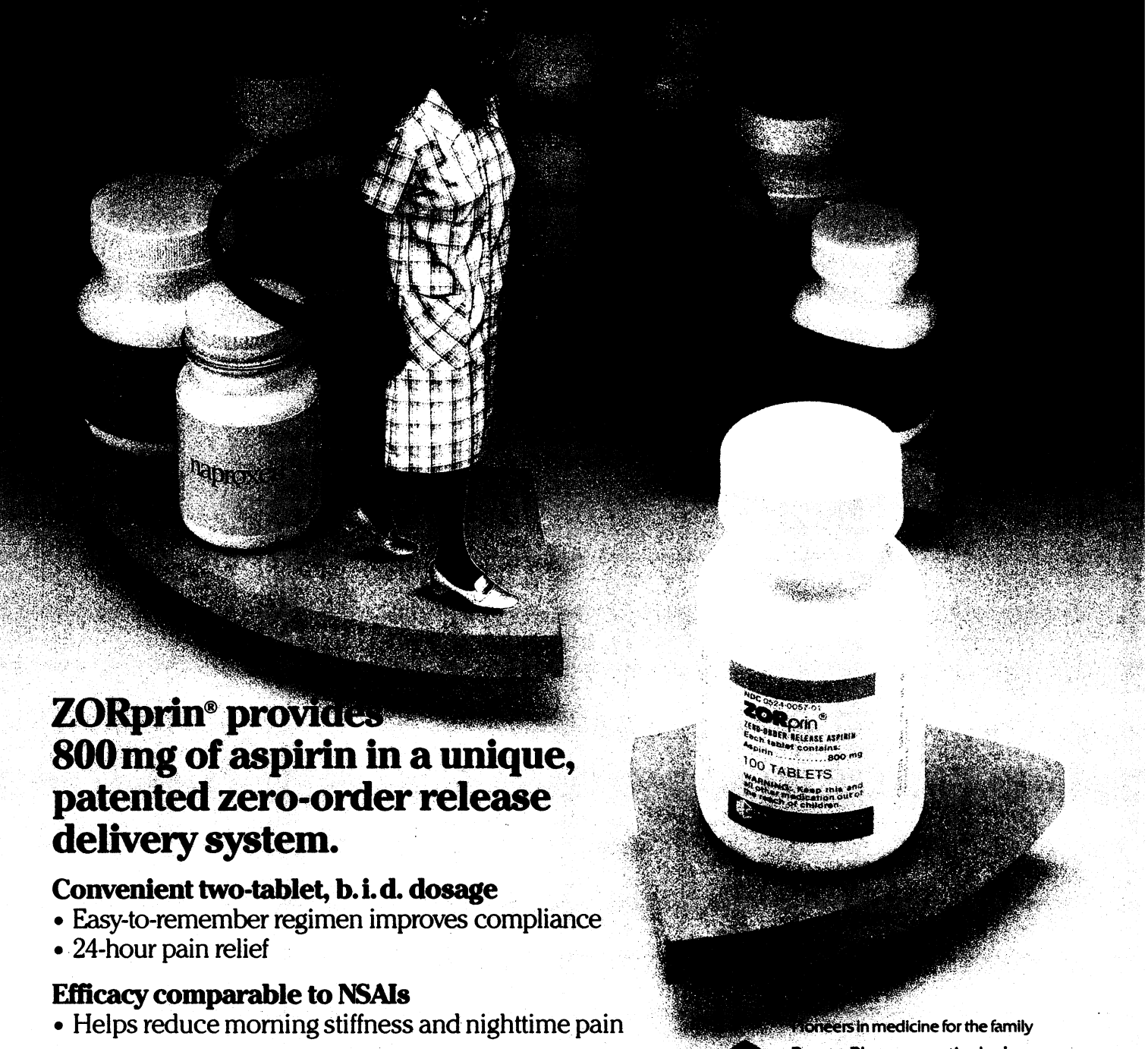
Cardizem 30-mg tablets are supplied in bottles of 100 (NDC 0088-1771-47) and in Unit Dose Identification Paks of 100 (NDC 0088-1771-49). Each green tablet is engraved with MARION on one side and 1771 engraved on the other. CARDIZEM 60-mg scored tablets are supplied in bottles of 100 (NDC 0088-1772-47) and in Unit Dose Identification Paks of 100 (NDC 0088-1772-49). Each yellow tablet is engraved with MARION on one side and 1772 on the other.

Issued 4/1/84

Another patient benefit product from

PHARMACEUTICAL DIVISION
MARION LABORATORIES, INC.
KANSAS CITY, MISSOURI 64137

Put ZORprin (ASPIRIN) Zero-Order Release in your circle of arthritic therapy



ZORprin® provides 800 mg of aspirin in a unique, patented zero-order release delivery system.

Convenient two-tablet, b.i.d. dosage
- Easy-to-remember regimen improves compliance
- 24-hour pain relief

Efficacy comparable to NSAIs
- Helps reduce morning stiffness and nighttime pain

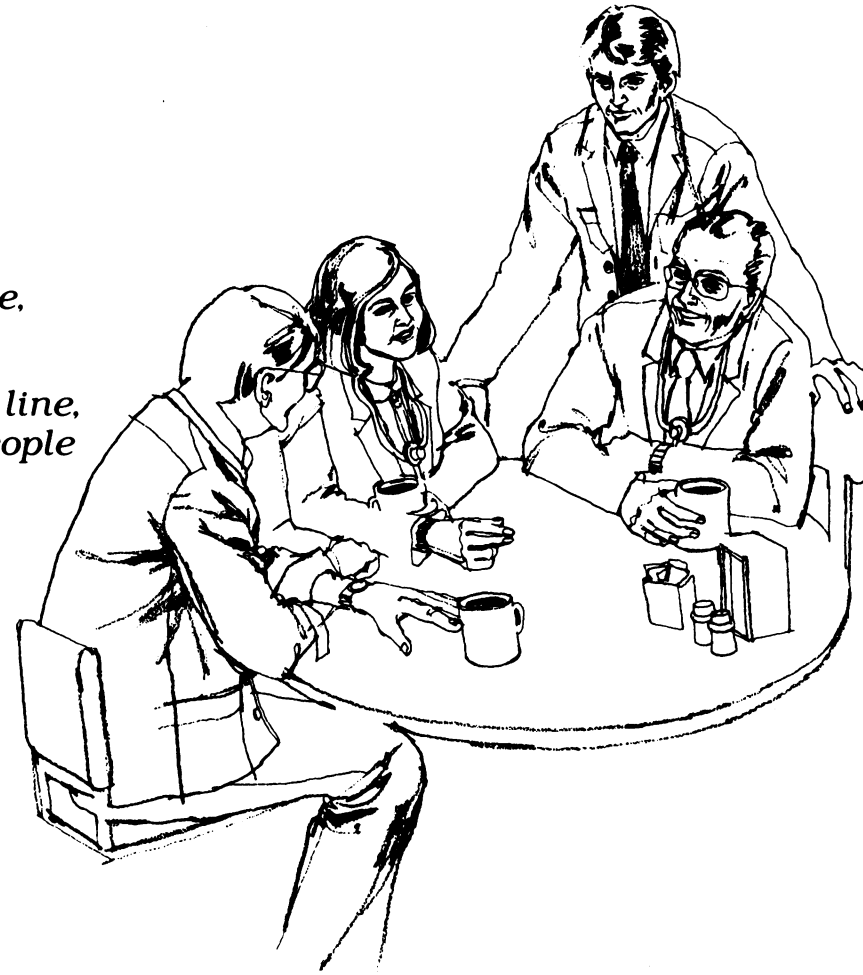
Side effect profile superior to plain aspirin... comparable to NSAIs
- ZORprin® is economical arthritic therapy
- Prescription only

The ideal method to maintain therapeutic control

Pioneers in medicine for the family

Boots Pharmaceuticals, Inc.
6540 LINE AVENUE, P.O. BOX 6750
SHREVEPORT, LOUISIANA 71106-9989

See brief summary of prescribing information on next page.



"When that summons came, I was glad I had SCPIE.

"My reputation was on the line, but SCPIE had the right people to handle everything.

"They know how to protect a physician."

Experience and strong physician management help make SCPIE Number One.

SCPIE is the largest Medical Association/Society-sponsored, physician-owned writer of claims made professional liability insurance in the nation!

This means:

Rates at the lowest possible level consistent with a stable company. The physician gets back premium dollars, plus investment income, not needed to pay claims and costs.

Already insured?

Ask about SCPIE's nose coverage. It lets qualified physicians move from another claims made carrier without paying "tail" coverage to the prior company. You join SCPIE at a premium commensurate with your rate and years of coverage under the prior plan.

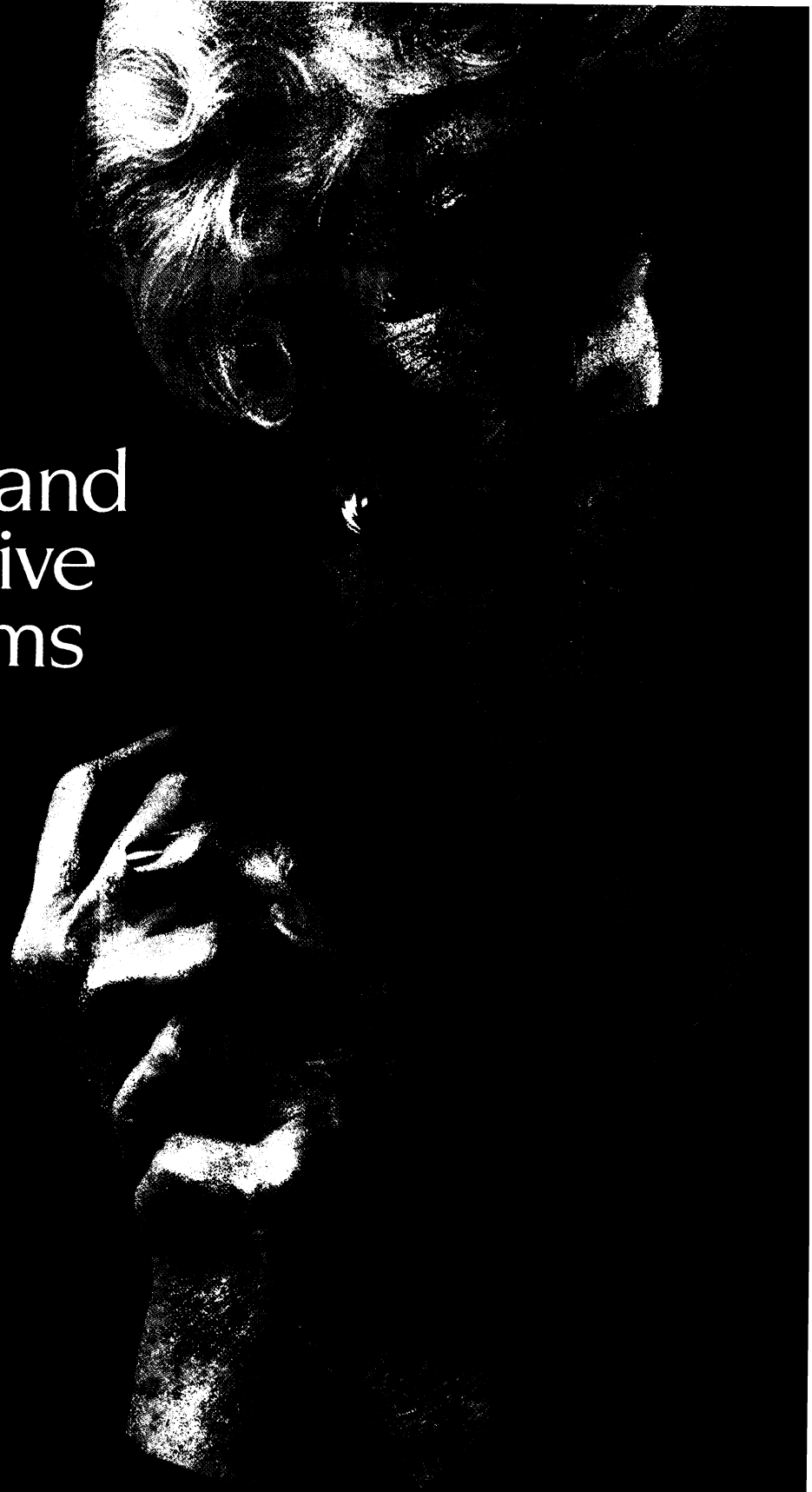
scpie

Southern California
Physicians Insurance
Exchange

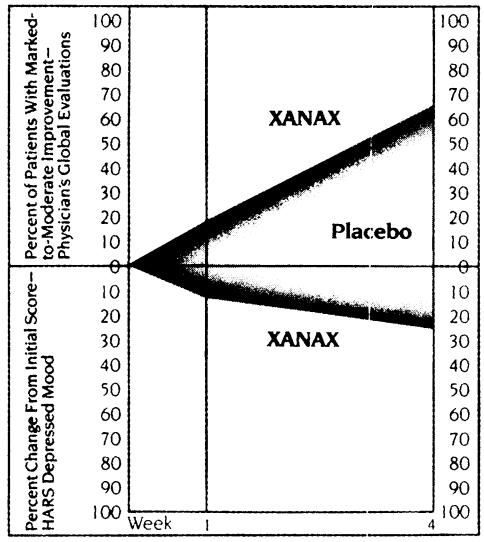
2029 Century Park East
Suite 2300
Los Angeles, CA 90067
(213) 552-8900

In 7 of 10
anxious
geriatrics...

Anxiety and depressive symptoms go hand in hand.



Xanax rapidly relieves anxiety with depressive symptoms.



In a recent clinical study[1] of 83 geriatric patients with clinical anxiety, 73% were diagnosed as having symptoms of depressed mood.

XANAX is well suited for therapy because it demonstrates greater efficacy than placebo in reducing the Hamilton Anxiety Rating Scale Total Score and individual items including depressed mood (see Figure).

With clinical advantages for geriatric patients.

- **Rapidly relieves** the symptoms of anxiety
- **Rapidly relieves** associated depressed mood
- **Well tolerated**—mild, transient drowsiness, the most commonly reported side effect the first week of therapy, shows a marked decrease thereafter and is not significantly different from that of placebo
- **Does not cause** cardiotoxicity
- **Specific geriatric dosage**—0.25 mg, two or three times daily

1. Cohn JB: Double-blind safety and efficacy comparison of alprazolam and placebo in the treatment of anxiety in geriatric patients. *Curr Ther Res* 1984;35(1):100-112.

Xanax® 0.25 mg Tablets

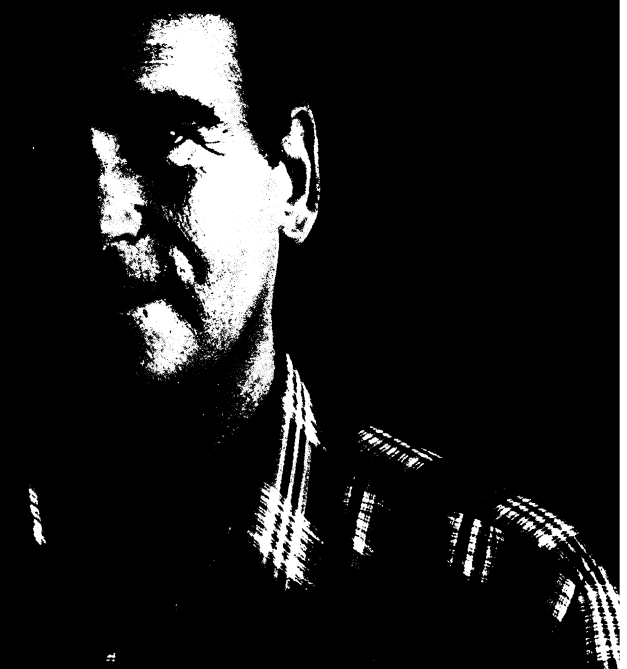
C IV

Upjohn THE UPJOHN COMPANY
Kalamazoo, Michigan 49001 USA

Please see next page for brief summary of prescribing information.

In Hypertensives Over 50, Diuretics Are Preferred

The 1984 Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure recommends diuretics as the favored monotherapy in patients over 50 years of age, regardless of sex or race.



Beta Blockers Aren't for Everyone...

For Hypertensive Patients*Over 50

P R E S C R I B E®

25 mg Hydrochlorothiazide/**50 mg** Triamterene/SKF

Used with Confidence for over 19 Years

Serum K^+ and BUN should be checked periodically (see Warnings and Precautions).

Before prescribing, see complete prescribing information in SK&F CO. literature or *PDR*. The following is a brief summary.

* **WARNING**

This drug is not indicated for initial therapy of edema or hypertension. Edema or hypertension requires therapy titrated to the individual. If this combination represents the dosage so determined, its use may be more convenient in patient management. Treatment of hypertension and edema is not static, but must be reevaluated as conditions in each patient warrant.

Contraindications: Concomitant use with other potassium-sparing agents such as spironolactone or amiloride. Further use in anuria, progressive renal or hepatic dysfunction, hyperkalemia. Pre-existing elevated serum potassium. Hypersensitivity to either component or other sulfonamide-derived drugs.

Warnings: Do not use potassium supplements, dietary or otherwise, unless hypokalemia develops or dietary intake of potassium is markedly impaired. If supplementary potassium is needed, potassium tablets should not be used. Hyperkalemia can occur, and has been associated with cardiac irregularities. It is more likely in the severely ill, with urine volume less than one liter/day, the elderly and diabetics with suspected or confirmed renal insufficiency. Periodically, serum K^+ levels should be determined. If hyperkalemia develops, substitute a thiazide alone, restrict K^+ intake. **Associated widened QRS complex or arrhythmia requires prompt additional therapy.** Thiazides cross the placental barrier and appear in cord blood. Use in pregnancy requires weighing anticipated benefits against possible hazards, including fetal or neonatal jaundice, thrombocytopenia, other adverse reactions seen in adults. Thiazides appear and triamterene may appear in breast milk. If their use is essential, the patient should stop nursing. Adequate information on use in children is not available. Sensitivity reactions may occur in patients with or without a history of allergy or bronchial asthma. Possible exacerbation or activation of systemic lupus erythematosus has been reported with thiazide diuretics.

Precautions: The bioavailability of the hydrochlorothiazide component of 'Dyazide' is about 50% of the bioavailability of the single entity. Theoretically, a patient transferred from the single entities of Dyrenium (triamterene, SK&F CO.) and hydrochlorothiazide may show an increase in blood pressure or fluid retention. Similarly, it is also possible that the lesser hydrochlorothiazide bioavailability could lead to increased serum potassium levels. However, extensive clinical experience with 'Dyazide' suggests that these conditions have not been commonly observed in clinical practice. Do periodic serum electrolyte determinations (particularly important in patients vomiting excessively or receiving parenteral fluids, and during concurrent use with amphotericin B or corticosteroids or corticotropin [ACTH]). Periodic BUN and serum creatinine determinations should be made, especially in the elderly, diabetics or those with suspected or confirmed renal insufficiency. Cumulative effects of the drug may develop in patients with impaired renal function. Thiazides should be used with caution in patients with impaired hepatic function. They can precipitate coma in patients with severe liver disease. Observe regularly for possible blood dyscrasias, liver damage, other idiosyncratic reactions. Blood dyscrasias have been reported in patients receiving triamterene, and leukopenia, thrombocytopenia, agranulocytosis, and aplastic and hemolytic anemia have been reported with thiazides. Thiazides may cause manifestation of latent diabetes mellitus. The effects of oral anticoagulants may be decreased when used concurrently with hydrochlorothiazide; dosage adjustments may be necessary. Clinically insignificant reductions in arterial responsiveness to norepinephrine have been reported. Thiazides have also been shown to increase the paralyzing effect of nondepolarizing muscle relaxants such as tubocurarine. Triamterene is a weak folic acid antagonist. Do periodic blood studies in cirrhotics with splenomegaly. Antihypertensive effects may be enhanced in post-sympathectomy patients. Use cautiously in surgical patients. Triamterene has been found in renal stones in association with the other usual calculus components. Therefore, 'Dyazide' should be used with caution in patients with histories of stone formation. A few occurrences of acute renal failure have been reported in patients on 'Dyazide' when treated with indomethacin. Therefore, caution is advised in administering nonsteroidal anti-inflammatory agents with 'Dyazide'. The following may occur: transient elevated BUN or creatinine or both, hyperglycemia and glycosuria (diabetic insulin requirements may be altered), hyperuricemia and gout, digitalis intoxication (in hypokalemia), decreasing alkali reserve with possible metabolic acidosis. 'Dyazide' interferes with fluorescent measurement of quinidine. Hypokalemia is uncommon with 'Dyazide', but should it develop, corrective measures should be taken such as potassium supplementation or increased dietary intake of potassium-rich foods. Corrective measures should be instituted cautiously and serum potassium levels determined. Discontinue corrective measures and 'Dyazide' should laboratory values reveal elevated serum potassium. Chloride deficit may occur as well as dilutional hyponatremia. Concurrent use with chlorpropamide may increase the risk of severe hyponatremia. Serum PBI levels may decrease without signs of thyroid disturbance. Calcium excretion is decreased by thiazides. 'Dyazide' should be withdrawn before conducting tests for parathyroid function.

Thiazides may add to or potentiate the action of other antihypertensive drugs.

Diuretics reduce renal clearance of lithium and increase the risk of lithium toxicity.

Adverse Reactions: Muscle cramps, weakness, dizziness, headache, dry mouth; anaphylaxis; rash, urticaria, photosensitivity, purpura, other dermatological conditions; nausea and vomiting, diarrhea, constipation, other gastrointestinal disturbances; postural hypotension (may be aggravated by alcohol, barbiturates, or narcotics). Necrotizing vasculitis, paresthesias, icterus, pancreatitis, xanthopsia and respiratory distress including pneumonitis and pulmonary edema, transient blurred vision, sialadenitis, and vertigo have occurred with thiazides alone. Triamterene has been found in renal stones in association with other usual calculus components. Rare incidents of acute interstitial nephritis have been reported. Impotence has been reported in a few patients on 'Dyazide', although a causal relationship has not been established.

Supplied: 'Dyazide' is supplied as a red and white capsule, in bottles of 1000 capsules; Single Unit Packages (unit-dose) of 100 (intended for institutional use only); in Patient-Pak™ unit-of-use bottles of 100.

BRS-DZ:L39

a product of

SK&F CO.

Carolina, P.R. 00630

The unique red and white Dyazide® capsule: Your assurance of SK&F quality.

Utah State Medical Association Annual Meeting

September 25-27, 1985

Westin Hotel Utah, Salt Lake City

Changes will continue to take place as "Medicine Moves Ahead in the Eighties." The meeting theme this year calls attention to the special Forum on Medical Issues which will bring together nationally prominent speakers to address issues in government, medical ethics, hospitals, and physician practice patterns.

Forum on Medical Issues

Thursday, September 26, 1985

(CME Credit 3 Hours)

Carolyne K. Davis, R.N., Ph.D.

Administrator of the Health Care Financing Administration (HCFA), Dr. Davis oversees the functions of the Medicare and Medicaid programs. HCFA helps to finance health care services for 50 million poor, elderly and disabled Americans with a budget over $90 billion in 1985.

Scott S. Parker, M.H.A.

Mr. Parker has held positions with health care institutions on both a state and national level. He is president of the American Hospital Association, a past member of the Board of Trustees, and past chairman of Associated Hospital Systems.

Ernlé W. D. Young, Ph.D.

Chaplain at the Stanford University Medical Center, Dr. Young is a senior lecturer on medical ethics. With a worldwide perspective, Dr. Young is well informed on ethical conflicts currently facing medicine.

Joseph F. Boyle, M.D.

Past president of the American Medical Association and Executive Director of ASIM. Dr. Boyle was chairman for the Health Agenda for the American People. A captivating speaker, Dr. Boyle brings to the forum the perspective of physicians and the challenges they will face in the modern medical marketplace.

Physician Reactor Panel

Following presentations by Forum speakers, questions and interaction with a physician panel will take place.

Panel Members:

Kim A. Bateman, M.D., practicing family physician and immediate past president of the Utah State Medical Association, member of the AMA Young Physicians Committee.

Alan R. Nelson, M.D., practicing physician in internal medicine, member of the AMA Board of Trustees and member of the Governing Council of the Institute of Medicine, National Academy of Sciences.

John C. Nelson, M.D., practicing obstetrician and gynecologist, member of the National Commission for review of the DRG System, member of a Steering Committee for the Health Agenda for the American People.

William D. Odell, M.D., professor of medicine and physiology, chairman of the Department of Medicine, University of Utah.

USMA House of Delegates

Wednesday, September 25, 1985

The House will commence with delegates meeting Wednesday morning for consideration of resolutions, reports and election of officers.

Reference committee meetings will also be held Wednesday morning followed by a luncheon for delegates.

Thursday, September 26, 1985

The House will reconvene to hear reports from reference committees and election results.

Special Events

Wednesday, September 25, 1985

The Hospital Medical Staff Section will meet prior to the USMA House of Delegates.

Luncheon with guest speaker:
John J. Coury, Jr., M.D.
Chairman, Board of Trustees
American Medical Association

Thursday, September 26, 1985

Luncheon with guest speaker:
Scott S. Parker, M.H.A., President
American Hospital Association

Presidents' Reception and Banquet
Lafayette Ballroom, Hotel Utah

Marketing Strategies for Private Practice

Friday, September 27, 1985

(CME Credit 2 Hours)

The business side of medical practice will be reviewed in a special AMA practice management seminar. You will learn practical ways to increase your patient load and maintain satisfaction with existing patients.

Seminar is useful for physicians just entering practice as well as those who are well established.

Course is limited to 50 participants. Cost: $75.00

Scientific Program

Friday, September 27, 1985

(CME Credit 3 Hours)

This exceptional half-day course provides a medical update on heart and vascular disease. The Scientific session is sponsored by Hoechst-Roussel Pharmaceuticals, Inc.

Cost Effective Use of Antimicrobials

Steven R. Jones, M.D.
Department of Medicine
Good Samaritan Hospital and Medical Center
Portland, Oregon

New Aspects of Treatment — Chronic Peripheral Vascular Disease

D. Eugene Strandness, M.D.
Professor of Surgery
University of Washington School of Medicine
Seattle, Washington

Use of Thrombolytic Therapy in Myocardial Infarction

William John Rogers, Jr., M.D.
Director, Myocardial Infarction Research Unit
UAB Medical Center
Birmingham, Alabama

Computer Workshops

Friday, September 27, 1985

(CME Credit 7 Hours)

Computer industry and American Medical Association surveys indicate that computer ownership by physicians will steadily increase throughout the 1980's. "User friendly" systems are rapidly developing that make office-based computer systems a necessity. USMA will present the second annual computer seminar all day on Friday, September 27. Cutting-edge information and outstanding teachers will be available for Utah physicians.

Topics will include:

Computers in Medical Practice: An Introduction
Physicians' User Panel Presentation
Computer Communication
Paperless Billing
The Paperless Office
Clinical Software
Computers in Medical Practice Made Easy
Integrated Academic Information Management System

Registration: No registration fee for USMA members
Nonmembers $50 • Thursday Luncheon $10 • Presidents' Banquet $50 per couple

For further information or registration material, please contact Utah State Medical Association, 540 East Fifth South, Salt Lake City 84102. Telephone (801) 355-7477.

WSMA

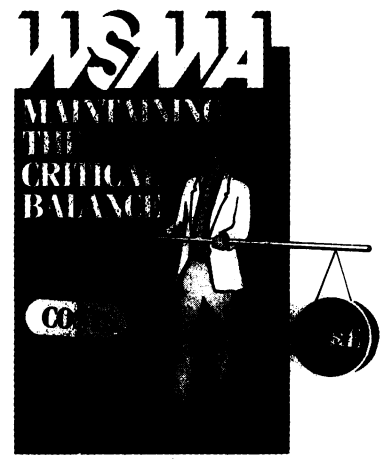
WASHINGTON STATE MEDICAL ASSOCIATION

MEETING FOCUSES ON CHANGE AND CHALLENGES

MAINTAINING THE CRITICAL BALANCE BETWEEN COSTS AND CARE will be an important theme of the 1985 WSMA Annual Meeting, September 19-22, Thunderbird Motor Inn, Jantzen Beach.

In addition to House of Delegates sessions which will shape future WSMA action on issues, including professional liability, the event-packed four-day meeting will feature a strong social-economic program and comprehensive scientific program.

All WSMA members are invited to attend.



ANNUAL MEETING
SEPTEMBER 19-22, 1985

SEPTEMBER 19-22, 1985

THUNDERBIRD MOTOR INN, JANTZEN BEACH, PORTLAND

SCIENTIFIC PROGRAMS

SURGERY	Prostate Imaging Using Transrectal Ultrasound, Plastic Surgery Symposium on Breast Reconstruction, Newer Aspects in Plastic Surgery
PSYCHIATRY	Post-traumatic Stress Disorder, Couples Therapy, WSPA Business Meeting
EMERGENCY MEDICINE	Chest Trauma in the Multiple Injury Patient, Post-Cardiac Arrest Cerebral Resuscitation, Thrombolytic Agents in Acute Myocardial Infarction, Free Standing Emergency Centers
ALLERGY	Recent Advances in Allergy and Clinical Immunology (for the non-specialist)
INTERNAL MEDICINE	Thrombolytic Therapy in Acute Myocardial Infarction, Update on AIDS, Pre-Thrombotic States and the Management of Venous Thrombosis, ACP: Health and Public Policy, ASIM Activities; An Update, Osteoporosis, Chronic Hepatitis, Flexible Sigmoidoscopy-1985, Ethics and Health Care Choices, Physician Reimbursement Issues, Rheumatology Session
OPHTHALMOLOGY	Scientific Program to be Announced, Choices for the Future of Ophthalmology, Joint Board Meeting (Washington and Oregon), Ophthalmic Assistants' Program (3 hour course on refraction)
FAMILY PRACTICE	Program to be Announced

A complete copy of the scientific program and annual meeting program is available from the Washington State Medical Association, 2033 Sixth Avenue, #900, Seattle, WA 98121, (206) 441-9762

Annual Meeting Speakers Varied, Provocative

An innovative no-fault approach to tort reform will be presented by Jeffrey O'Connell, professor of law at the University of Virginia. O'Connell specializes in accident and insurance law. He has authored numerous books including a 1979 work, "The Lawsuit Lottery: Only the Lawyers Win." O'Connell will speak to the House of Delegates on Thursday morning, 11:00 a.m.

Harry E. Morgan, Jr., chairman of the Health Care Purchasers Association of Puget Sound, will also address the House. He will discuss "A Business Prospectus on the Cost of Health Care."

Thursday afternoon Susan M. Schmidt, counsel to the special AMA Task Force on Professional Liability which has produced a series of reports on the issue, will join O'Connell and Morgan on a special reference committee panel. The panel will further review the liability issue and invite physician comment.

Dr. Roy M. Schwarz, AMA vice president of medical education and science policy, will address meeting attendees on Friday morning on the future direction of medical education and major science issues facing American medicine in the future.

If you would like additional information regarding the 96th WSMA Annual Meeting, detach and return the completed form below:

Return to:
Washington State Medical Association
2033 Sixth Avenue, #900
Seattle, WA 98121

Please send me more detailed information on the 1985 Washington State Medical Association Annual Meeting

Name

Address

City *State* *Zip*

96th ANNUAL MEETING

Classified Advertisements

The rate for each insertion is $5 per line (average six words per line) with five line ($25) minimum. Box number charge: $5 each month.

Classified display rates $50 per inch.

Copy for classified advertisements should be received not later than **the first of the month preceding issue. All copy must be typed or printed.** • Classified advertisers using Box Numbers forbid the disclosure of their identity. Your inquiries in writing will be forwarded to Box Number advertisers. The right is reserved to reject or modify all classified advertising copy in conformity with the decisions of the Advertising Committee.

Please Type or Print Advertising Copy

Classified Advertisements Are Payable in Advance

THE WESTERN JOURNAL OF MEDICINE
44 GOUGH STREET, SAN FRANCISCO, CA 94103

PHYSICIANS WANTED

FAMILY PRACTICE PHYSICIAN to join 15 physician multispecialty group located in Southern Idaho. Send résumé to Business Administrator, Box 1233, Twin Falls, ID 83301.

FAMILY PRACTICE opportunity in eastern New Mexico. Join two physicians in private practice situation with an established patient population. Must do OB. No buy-in; just share expenses and call. Family community with stable economy. Contact Bill Norris, Southwest Community Health Services, PO Box 26666, Albuquerque, NM 87125-6666, or call 1 (800) 545-4030, ext. 3050.

ACADEMIC GENERAL INTERNISTS, CARDIOLOGIST, AND ENDOCRINOLOGIST, DO—Wanted for full-time faculty positions. Must be Board admissible or certified, interested in teaching medical students and house staff. Good balance between clinical practice and teaching with research opportunities available. Assistant Professor level with excellent guaranteed salary and benefits. Send CV to Victor H. Kaylarian, DO, Department of Medicine, University of Osteopathic Medicine and Health Sciences, 3200 Grand Ave., Des Moines, IA 50312. All inquiries confidential.

KETCHUM, SUN VALLEY, IDAHO: Internist, Surgeon, Pediatrician, Orthopedist in multispecialty, expanding, well-equipped clinic. Income moderate; quality of life highest. Dr Bryan Stone, PO Box 2198, Ketchum, ID 83340; (208) 726-9361.

HEMATOLOGIST-ONCOLOGIST to join Oncologist in progressive multispecialty group practice located in suburban San Francisco area. University affiliation and NCOG protocol participation encouraged. Competitive salary and benefits leading to partnership. Send résumé to Box 6479, The Western Journal of Medicine, 44 Gough St., San Francisco, CA 94103.

FAMILY PRACTICE-INTERNAL MEDICINE-SURGEON. Multispecialty clinic in Northern Idaho Panhandle. Nominal lease includes fully-equipped office and treatment suites with receptionist and janitorial services provided. Clinic includes lab, x-ray and pharmacy. Billing services available. Located in a four-season playground rich with forests, lakes, streams and wild game. Just 20 minutes from a 14-run ski resort. Attractive lifestyle. For information: (208) 784-1221, ext. 304. Mail résumé to: Shoshone Medical Center, Jacobs Gulch, Kellogg, ID 83837.

GENERAL/ORTHOPEDIC SURGEON/FP/-INTERNIST to join multispecialty group in New Mexico. Excellent benefit package. First year salary guarantee negotiable. Well-equipped private outpatient clinic. Five minutes from new hospital. Call Mr. Miller or write 114 West 11th St., Silver City, NM 88061; (505) 388-1511, or (505) 538-2408 in evenings.

PHYSICIANS WANTED

SOUTHERN CALIFORNIA

Prestigious HMO is seeking experienced specialists and general practitioners for our facilities in Los Angeles and Orange Counties. Located in close proximity to major teaching centers, we offer the opportunity for continued professional development and rewarding clinical practice. Excellent compensation and benefits including paid malpractice, life, disability, medical and dental coverage, paid vacations, sick leave, educational leave and retirement plan. Please send CV to: Director/Physician Recruitment, CIGNA Healthplans of California, 700 North Brand Blvd., Suite 500-49, Glendale, CA 91203.

FAMILY PRACTICE at scenic Lake Chelan, WA. Join 3 other BC FPs, share call, expenses and building. Obstetrics required. Nearly new hospital. Gross 180-200K. Extensive recreational opportunities available. Practice for sale for modest negotiable amount or possibly available on a salaried basis. Contact Lake Chelan Clinic, PO Box 368, Chelan, WA 98816; (509) 682-2511.

NORTHERN CALIFORNIA: Physician, Board certified/eligible in Emergency Medicine or Family Practice, to work part-time or full-time in busy free-standing emergency center. Competitive compensation and malpractice paid. Send CV and references to Joanne Berkowitz, MD, The Emergency Center Medical Group, 4948 San Juan Ave., Fair Oaks, CA 95628.

FAMILY PRACTITIONER—TULARE COUNTY, CALIFORNIA: Board certified/eligible Family Practitioner to practice in an out-patient clinic, which includes in-patient duties, with 13 physicians. Consider a semi-rural lifestyle with cultural amenities, the Coast and the Sierra Nevada Mountains easily accessed. Salary: $81,236-$85,376 annually. The County provides a benefit package which includes malpractice insurance coverage. Send CV to Tulare County Personnel, Courthouse, Room 106, Visalia, CA 93291; (209) 733-6266. An Affirmative Action Employer.

CALIFORNIA—Physicians interested in fulltime practice in Urgent Care Center at Palo Alto Medical Foundation. Must be residency trained and Board Certified in FP, IM, General Surgery, Occupational Medicine or Emergency Medicine. ACLS Certified. Must be experienced in a wide variety of out-patient Medical/Surgical skills in adults and children. Occupational Medicine experience desirable. Salary, vacation, meeting time; malpractice, dental, medical, disability insurance; three year track for partnership. Available July/August 1985. For information send CV to: William E. Straw, MD, Medical Director, Urgent Care Center, Palo Alto Medical Foundation, 300 Homer Ave., Palo Alto, CA 94301. Please reply Box 6484, Western Journal of Medicine, 44 Gough St., San Francisco, CA 94103.

PHYSICIANS WANTED

IMMEDIATE OPENING—Opportunity for Internist, Cardiologist or Family Practice to join two doctor clinic grossing near $400,000. Opportunity to buy in also. Two Surgeons and over five Family Practice Doctors who will support an Internist. Central WA; (509) 422-2600.

CALIFORNIA—Board Certified/eligible or residency trained emergency physician wanted to join 320 physician multispecialty group. Competitive salary and excellent fringe benefits. Ninety miles from Sierra skiing and San Francisco. California license required. Send curriculum vitae to Mrs. Carolyn Whelan, The Permanente Medical Group, Inc., PO Box 254999, Sacramento, CA 95825. An equal opportunity employer.

WASHINGTON COASTAL COMMUNITY serving a population of 65,000 is actively recruiting the following specialists: ENT, Urologist, Orthopedic Surgeon, General Surgeon. A variety of practice support options are available, i.e., office space, relocation assistance, etc. Enjoy the support of major West Coast Catholic Hospital System. Community has close proximity to major recreational areas and easy access to Seattle and Portland. For information send CV and references to: Nancy Friedrich, The Friedrich Group, 9284 Ferncliff North East, Bainbridge Island, WA 98110.

CALIFORNIA, RURAL AMERICAN AND OVERSEAS: Primary care physicians and OB/GYN needed for locum and permanent placements in CA, Saudi Arabia and, southwestern US. Excellent financial package, practice management and affiliation with a dynamic healthcare company. CV to: Beverly Froley, Westworld Healthcare Resources, 23832 Rockfield Rd., Lake Forest, CA 92630; (800) 847-1596.

CHAIRPERSON, DEPARTMENT OF SURGERY: The Permanente Medical Group is taking applications for the position of chairperson for the Department of Surgery at our Oakland Medical Center. The Oakland facility is a 330-bed acute care teaching hospital with a five-year general surgery residency program. The Surgery Department is composed of seven board certified general surgeons; two having completed vascular fellowships. Interested candidates must be board certified and prior experience with resident training programs preferred. Please send curriculum vitae to: Richard Brown, MD, Chairman, Search Committee, Kaiser Permanente Medical Group, Inc., 280 West MacArthur Blvd., Oakland, CA 94611.

CARDIOLOGIST: To join two busy invasive Cardiologists in the beautiful Pacific Northwest. Practice includes open heart surgery program, PTCA. Requires catheterization and all non-invasive modalities. EPS and PTCA would be a plus. Please reply with a CV to Box 6487, Western Journal of Medicine, 44 Gough St., San Francisco, CA 94103.

URGENT CARE CLINIC: Sacramento, CA. Full time family practice oriented emergency physician. Twelve hours/day. Gurarantee plus percentage. Malpractice provided. Minimum one year commitment. Please reply to Box 6485, Western Journal of Medicine, 44 Gough St., San Francisco, CA 94103.

MONTANA FAMILY PRACTICE: Have the best of both worlds. BE/BC Family Practitioner needed to establish a Department of Family Practice as part of The Billings Clinic—a 62-physician multispecialty group. Enjoy practice with or without obstetrics in a regional medical center with subspecialty backup and the cultural advantages of good schools, art, drama, symphony orchestra, etc. You and your family can enjoy the wide open spaces together. There is riding, fishing, hiking, skiing, hunting, canoeing, to name a few. This is a delightful place to raise a family. Salary leading to partnership. Contact: Paul V. Hoyer, MD, The Billings Clinic, PO Box 35100, Billings, MT 59107-5100. Telephone (406) 256-2500.

AMBULATORY CARE: Associate wanted. Prefer Board certified or eligible FP, EM, IM with interest in acute care for ambulatory/minor emergency center. Full- or part-time with flexible scheduling. Partnership possible. Contact Roger Simms, MD, at Firstcare Medical Center, 5702 North 26th, Tacoma, WA 98407; (206) 759-6655.

(Continued on Page 292)

(Continued from Page 290)

PHYSICIANS WANTED

FACULTY MEMBER, ASSOCIATE PROFESSOR—Conduct university courses for licensed doctors and graduate medical students attempting to be certified by the State Acupuncture Board to practice herbology and acupuncture; teach subjects in technique and theory of acupuncture, practical application of herbal medicine within curriculum; deliver lectures; demonstrate acupuncture techniques; conduct research. Must be licensed Acupuncturist by the State of California. Must be able to take command of a classroom situation and transmit enthusiasm for course materials. Must possess AMD or OMD degree with one year experience in this job or one year related experience involving acupuncture treatment and therapeutics. $28,848 year. 40 hours/week. Job and interview in San Diego. Send a copy of this ad and your résumé re: job #1764 to PO Box 865, Sacramento, CA 95804, not later than 9/1/85.

CALIFORNIA, SAN JOAQUIN VALLEY: Personable BC/BP Emergency Medicine physician needed to associate with group of career Emergency Physicians in a progressive community, nonprofit hospital. Emergency Department is full department status, about 32,000 visits/year. Paramedic base station, trauma receiving hospital. Excellent support from consulting staff in all specialties including cardiac surgery. Interest in EMS desirable. Teaching position in Emergency Medicine Residency available. Generous financial arrangements with parity at two (2) years. Send CV in complete confidence to: PO Box 3893, Pinedale, CA 93650.

ONCOLOGIST BE/BC wanted for large HMO practice in northern California wine country. Reply with CV to Box 6489, Western Journal of Medicine, 44 Gough St., San Francisco, CA 94103.

OB/GYN: Board certified/eligible OB/GYN wanted to join fee-for-service multispecialty group on northern California redwood coast. Initial guarantee with immediate full partnership revenue participation, health and malpractice insurance. For additional information, please contact: Erika Quick, Administrator, Del Norte Medical Clinic Inc, 370 Ninth St., Crescent City, CA 95531; (707) 464-4116.

KNOWLEDGEABLE FP to be main practitioner and director of attractive, rapidly growing immediate medical care center. Guaranteed salary, plus percentage of gross (including lab x-ray and PT). Must be personable with excellent medical skills. Call Dr. Butler (213) 633-2273, 5203 Lakewood Blvd, Lakewod, CA

BC/BE PRIMARY CARE INTERNIST needed for community hospital-based teaching practice in East Los Angeles. Inpatient and office clinical and teaching responsibilities. Must qualify for medical school faculty appointment. California license. Competitive salary and benefits package. Bilingual English-Spanish preferred. Send CV to James Drinkard, MD, White Memorial Medical Group, 414 North Boyle Ave., Los Angeles, CA 90033.

FP/INTERNIST BC/BE for progressive Community Clinic in rural, coastal northern California. Join FP, Pediatrician, OB/GYN, FNP's and PA's in Family Medicine/Preventive Health practice. Salaried position with benefits, malpractice coverage. Pleasant university town, five minutes to hospital. Send CV/inquiries to Teresa Clark, Humboldt Open Door Clinic, Arcata, CA 95521; (707) 822-2957.

GENERAL INTERNAL MEDICINE SPECIALIST position open with 35 member multispecialty group. Excellent practice opportunity, full range of benefits, immediate shareholder status, all practice costs paid. For more information contact: Colin Wells, MD, Recruitment Coordinator, or David E. Graham, Associate Administrator, San Luis Medical Clinic, Ltd., 1235 Osos St., San Luis Obispo, CA 93401; (805) 546-5600.

IDAHO: Eight-man group seeking ninth physician. Live near skiing, fishing, hunting, and wilderness while practicing in two modern medical centers. One is a trauma center with active EMS system. Seeking experienced EM physician, preferably with administrative experience and EM certification. Competitive salary, malpractice, retirement, and other fringes. Reply PO Box 2572, Boise, ID 83701 or call (208) 322-1730.

PHYSICIANS WANTED

GENERAL PRACTITIONER needed for hospital in Northern Oregon. A basic 40 hour work week, 8 am to 5 pm per day plus rotating emergency call will be required. Salary offered is $120,000 for the first 24 months. MD degree and one year medical internship required. Interviewing and moving expenses are paid. Qualified candidates please send CV to: Employment Division, Attn: Job Order #1885172, 875 Union St. N.E., Room 208, Salem, OR 97311. Job Order #1885172.

SAN FRANCISCO (San Francisco County): Internal Medicine private practice opportunity available. Board certified/eligible, woman preferred. Practice established over 8 years, busy, excellent location in office building next to Children's Hospital, with housestaff, ER, all facilities close at hand. Versatile call schedule and opportunities for teaching available. Contact: Ann Fricker, MD, 3838 California St., Ste. 12, San Francisco, CA 94118; (415) 387-6171.

OREGON—GENERAL SURGEON sought for multispecialty group, serving 57,000 population area. Beautiful rural community, 38 miles from Portland. Send CV to ADM. Physicians' Medical Center, P.C., 420 East 5th St., McMinnville, OR 97128; (503) 472-6161.

WESTERN U.S. OPENINGS

Several multi-specialty groups and clinics have asked us to recruit for over 100 positions of various specialties.

Western States Physician Search
240 West Shaw, Suite C
Clovis, CA 93612
(209) 297-7748

DEPUTY HEALTH OFFICER—An outstanding opportunity offering an expanded preventive and public health experience involving community health programs, outpatient care and participation in medical and health care management. Enjoy a semi-rural lifestyle, a reasonable cost of living, access to cultural amenities, a competitive starting salary, liberal fringe benefits, a regular schedule, and no overhead costs. Requires possession of a valid Physician's and Surgeon's Certificate issued by the State of California. Recruitment period: 6/24/85 to 8/30/85, 5:00 pm. Applications may be obtained by contacting the Butte County Personnel Department, 25 County Center Dr., Oroville, CA 95965-3387; (916) 534-4651. An equal opportunity employer.

GASTROENTEROLOGIST BE/BC wanted for large HMO practice in northern California wine country. Reply with CV to Box 6488, Western Journal of Medicine, 44 Gough St., San Francisco, CA 94103.

LOCUM TENENS

LOCUM TENENS SERVICE
WESTERN PHYSICIANS REGISTRY

. . . offers coverage for vacation or continuing education. To arrange coverage for your practice or to participate as temporary physician, contact: **Carol Sweig, Director, 1124 Ballena, Alameda, CA 94501; (415) 521-4110.**

SKI AND WORK—Part-time ER experienced, ACLS certified physicians sought to staff ski area clinics in Nevada, Oregon and New Mexico. Financial remuneration and benefits! Send CV to: C. H. Fagan, MD, Box 5220, Playa del Rey, CA 90296 or call (213) 546-3107 for further details.

PRACTICES AVAILABLE

CALIFORNIA BAY AREA. Primary Care for sale. Established General Practice one hour to San Francisco. Area growing very rapidly. $100,000+ gross last 5 years. Asking $50,000 but very flexible, depending on amt. of equip I leave. Please reply Box 6490, Western Journal of Medicine, 44 Gough St., San Francisco, CA 94103.

PULMONARY DISEASE/ALLERGY practice in San Bernardino. Good lease, 1,400-foot office. Computer billing and Video patient educational systems, Pulmonary Function Laboratory euipment, trained assistant. Donald Thornton, MD, 1800 North Western Ave., 3406, San Bernardino, CA 92411; (714) 887-8088.

WELL ESTABLISHED GENERAL PRACTICE and free standing care center in Northern California for sale. Office fully equipped. Inquiries Box 6481, Western Journal of Medicine, 44 Gough St, San Francisco, CA 94103.

PRACTICES AVAILABLE

OB/GYN PRACTICE for sale in the Napa Valley. Solo private practice with call sharing with other OB/GYNs. $300,000 gross in 1984. 150 bed hospital with new Maternity Center. One hour from San Francisco. Available immediately. Will continue working for three to six months to assure successful transition. Contact: Lanita C. Witt, MD, 935 Trancas, Suite 4E, Napa, CA 94558; (707) 257-2571.

OPHTHALMOLOGY PRACTICE FOR SALE: 1985 or 1986. Pacific Northwest Coast. Office building for lease or sale. Retiring. Will stay to introduce. Reply including CV to Box 6472, Western Journal of Medicine, 44 Gough St., San Francisco, CA 94103.

CALIFORNIA: Otolaryngology, Pediatric, Psychiatric, Opthalmology, Allergy, OBG, Family, Internal, Surgery, Orthopedic, others. Contact Mary Bradshaw, Practice Broker/Recruiter, 21 Altamount Dr., Orinda, CA 94563; (415) 376-0762.

ORTHOPAEDIC PRACTICE—Orange County, California, adjacent to major hospital; five additional hospitals in 5-mile radius; will aid in transition. Box 4191, Irvine, CA 92714.

SAN DIEGO—General Surgeon, OB/GYN, MD to take prac/office. Best med area. Off sublease. 2 cnslt 2 exam lg rcrds rm bath etc. Frn/equip avail. (619) 287-0151 or PO Box 202053, San Diego, CA 92120-0925.

REAL ESTATE

SAN LEANDRO: Prime, central. Prestige medical building. Ample parking. *Great* opportunity Internist or GP. Carol Bull, (415) 357-8940.

CENTRAL CALIFORNIA Arroyo Grande. Long term leasehold space with option to buy. 2,000+ square feet in new professional complex. Available in October. Help design interior now. Construction allowance given. (213) 649-0036.

AVAILABLE NOW—Oxnard, Ventura County, California; newly constructed 3,458 square feet with seven exam rooms, three consultation, x-ray, physical therapy, minor surgery, laboratory, nurses station. Contact: Anna Bischof, (805) 485-3193.

VALLEJO, CALIFORNIA: Prelease space in this new medical office building to be constructed across the street from Sutter Hospital. Sutter is doing a 13 million dollar expansion to the present hospital, to include 51 new beds, doubling the intensive care unit and adding to the surgery section. Marine World Africa USA is under construction within one mile bringing more growth to the area. Vallejo is halfway between Sacramento and San Francisco; it's convenient to skiing, the ocean and lake water sports. Building can be ready for occupancy in six months. Call Joe Lillis at (707) 864-8524 or write PO Box 523, Fairfield, CA 94533 for more information.

SITUATIONS WANTED

RADIOLOGIST SEEKS POSITION—41-year-old experienced Radiologist (academics and private practice) seeks multispecialty group, solo-type practice, or imaging center. Reply Box 6486, Western Journal of Medicine, 44 Gough St., San Francisco, CA 94103.

OFFICE SPACE AVAILABLE

OFFICE SPACE TO SHARE—Southern California area. Fully equipped and staffed medical office to share, in Los Angeles area. Office is 1,100 square feet, and includes x-ray and lab facilities. (805) 526-4380.

MISCELLANEOUS

CONTRACT NEGOTIATION: Practicing physicians with ten years' experience in collective bargaining and corporate medical affairs. Non-union. Call (415) 461-2080 for further information or write to PMC, Box 1434, Ross, CA 94957. Reply in strictest confidence.

SERVICES

PATIENT NEWSLETTER: Keeping in touch shows that you care! Send for your free sample copy of our quarterly health promotion newsletter. Customized for you. Mailing service option. Rx: Live well, 6809 Santa Maria Ln., Dallas, TX 75214-2847 or call (214) 821-5218.

PROFESSIONAL RÉSUMÉ SERVICES. Curriculum vitae preparation for physicians. Prompt and confidential. Call toll free. 1 (800) 6-CAREER. In PA, (215) 433-4112.

New Prescribing Information

Before prescribing, please consult complete product information, a summary of which follows:

Indications: Relief of moderate to severe depression associated with moderate to severe anxiety.

Contraindications: Known hypersensitivity to benzodiazepines or tricyclic antidepressants. Do not use with monoamine oxidase (MAO) inhibitors or within 14 days following discontinuation of MAO inhibitors since hyperpyretic crises, severe convulsions and deaths have occurred with concomitant use; then initiate cautiously, gradually increasing dosage until optimal response is achieved. Contraindicated during acute recovery phase following myocardial infarction.

Warnings: Use with great care in patients with history of urinary retention or angle-closure glaucoma. Severe constipation may occur in patients taking tricyclic antidepressants and anticholinergic-type drugs. Closely supervise cardiovascular patients. (Arrhythmias, sinus tachycardia and prolongation of conduction time reported with use of tricyclic antidepressants, especially high doses. Myocardial infarction and stroke reported with use of this class of drugs.) Caution patients about possible combined effects with alcohol and other CNS depressants and against hazardous occupations requiring complete mental alertness (*e.g.*, operating machinery, driving).

***Usage in Pregnancy:* Use of minor tranquilizers during the first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.**

Since physical and psychological dependence to chlordiazepoxide have been reported rarely, use caution in administering Limbitrol to addiction-prone individuals or those who might increase dosage; withdrawal symptoms following discontinuation of either component alone have been reported (nausea, headache and malaise for amitriptyline; symptoms [including convulsions] similar to those of barbiturate withdrawal for chlordiazepoxide).

Precautions: Use with caution in patients with a history of seizures, in hyperthyroid patients or those on thyroid medication, and in patients with impaired renal or hepatic function. Because of the possibility of suicide in depressed patients, do not permit easy access to large quantities in these patients. Periodic liver function tests and blood counts are recommended during prolonged treatment. Amitriptyline component may block action of guanethidine or similar antihypertensives. Concomitant use with other psychotropic drugs has not been evaluated; sedative effects may be additive. Discontinue several days before surgery. Limit concomitant administration of ECT to essential treatment. See Warnings for precautions about pregnancy. Limbitrol should not be taken during the nursing period. Not recommended in children under 12. In the elderly and debilitated, limit to smallest effective dosage to preclude ataxia, oversedation, confusion or anticholinergic effects.

Adverse Reactions: Most frequently reported are those associated with either component alone: drowsiness, dry mouth, constipation, blurred vision, dizziness and bloating. Less frequently occurring reactions include vivid dreams, impotence, tremor, confusion and nasal congestion. Many depressive symptoms including anorexia, fatigue, weakness, restlessness and lethargy have been reported as side effects of both Limbitrol and amitriptyline. Granulocytopenia, jaundice and hepatic dysfunction have been observed rarely.

The following list includes adverse reactions not reported with Limbitrol but requiring consideration because they have been reported with one or both components or closely related drugs:

Cardiovascular: Hypotension, hypertension, tachycardia, palpitations, myocardial infarction, arrhythmias, heart block, stroke.

Psychiatric: Euphoria, apprehension, poor concentration, delusions, hallucinations, hypomania and increased or decreased libido.

Neurologic: Incoordination, ataxia, numbness, tingling and paresthesias of the extremities, extrapyramidal symptoms, syncope, changes in EEG patterns.

Anticholinergic: Disturbance of accommodation, paralytic ileus, urinary retention, dilatation of urinary tract.

Allergic: Skin rash, urticaria, photosensitization, edema of face and tongue, pruritus.

Hematologic: Bone marrow depression including agranulocytosis, eosinophilia, purpura, thrombocytopenia.

Gastrointestinal: Nausea, epigastric distress, vomiting, anorexia, stomatitis, peculiar taste, diarrhea, black tongue.

Endocrine: Testicular swelling and gynecomastia in the male, breast enlargement, galactorrhea and minor menstrual irregularities in the female, elevation and lowering of blood sugar levels, and syndrome of inappropriate ADH (antidiuretic hormone) secretion.

Other: Headache, weight gain or loss, increased perspiration, urinary frequency, mydriasis, jaundice, alopecia, parotid swelling.

Overdosage: Immediately hospitalize patient suspected of having taken an overdose. Treatment is symptomatic and supportive. I.V. administration of 1 to 3 mg physostigmine salicylate has been reported to reverse the symptoms of amitriptyline poisoning. See complete product information for manifestation and treatment.

Dosage: Individualize according to symptom severity and patient response. Reduce to smallest effective dosage when satisfactory response is obtained. Larger portion of daily dose may be taken at bedtime. Single *h.s.* dose may suffice for some patients. Lower dosages are recommended for the elderly.

Limbitrol DS (double strength) Tablets, initial dosage of three or four tablets daily in divided doses, increased to six tablets or decreased to two tablets daily as required. Limbitrol Tablets, initial dosage of three or four tablets daily in divided doses, for patients who do not tolerate higher doses.

How Supplied: *Double strength (DS) Tablets*, white, film-coated, each containing 10 mg chlordiazepoxide and 25 mg amitriptyline (as the hydrochloride salt), and *Tablets*, blue, film-coated, each containing 5 mg chlordiazepoxide and 12.5 mg amitriptyline (as the hydrochloride salt)—bottles of 100 and 500; Tel-E-Dose® packages of 100; Prescription Paks of 50.

ROCHE

ROCHE PRODUCTS INC.
Manati, Puerto Rico 00701

CLEARING:
BOTH DEPRES
AND ANXIETY...

Now

IN PLACE OF
LIMBITROL 5-12.5 WRITE: Limbitrol®

IN PLACE OF
LIMBITROL 10-25 WRITE: Limbitrol DS®

Easier to remember...easier to prescribe